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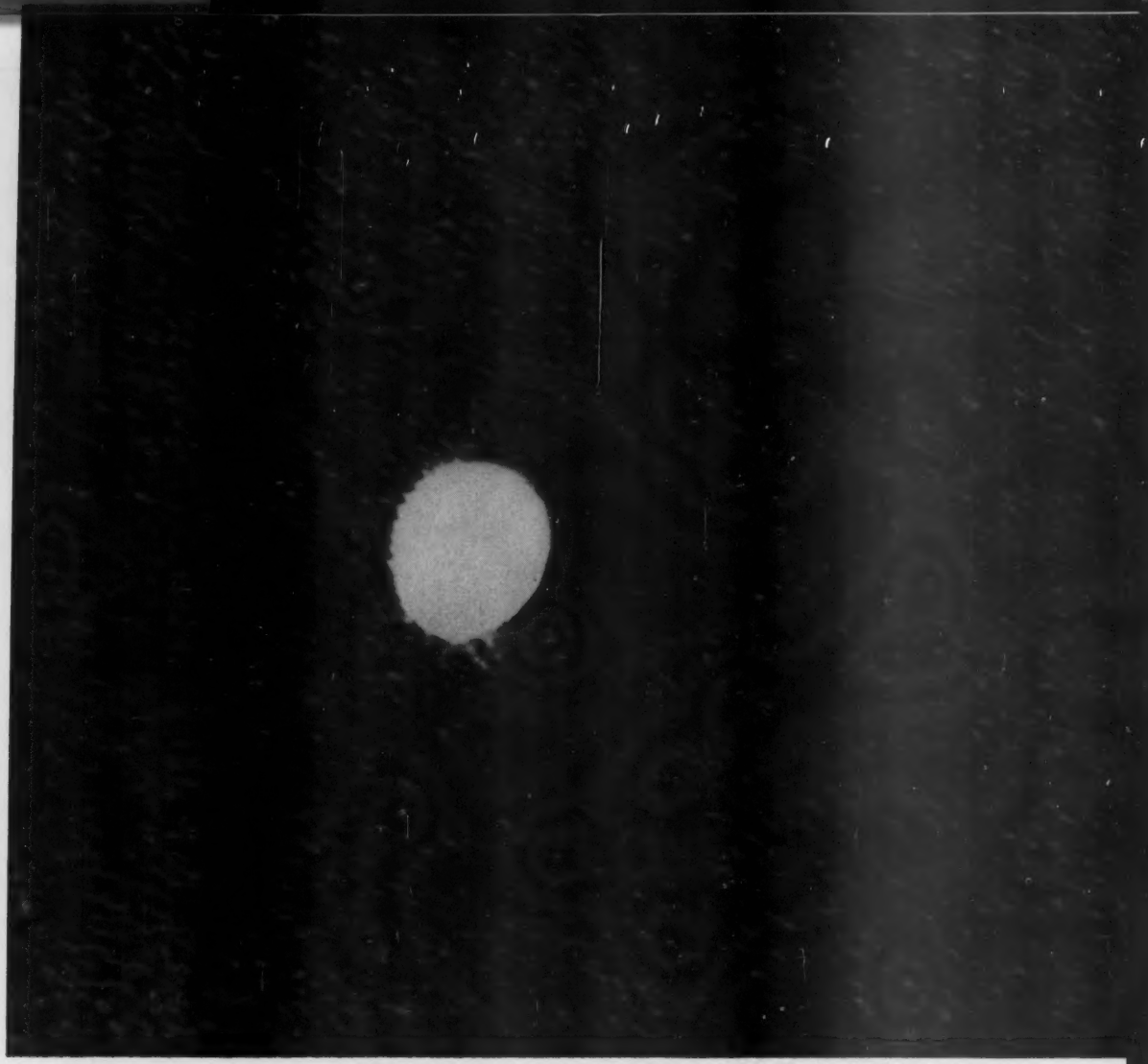

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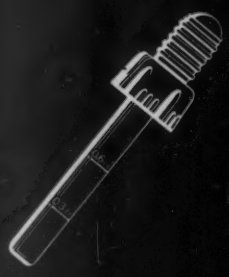

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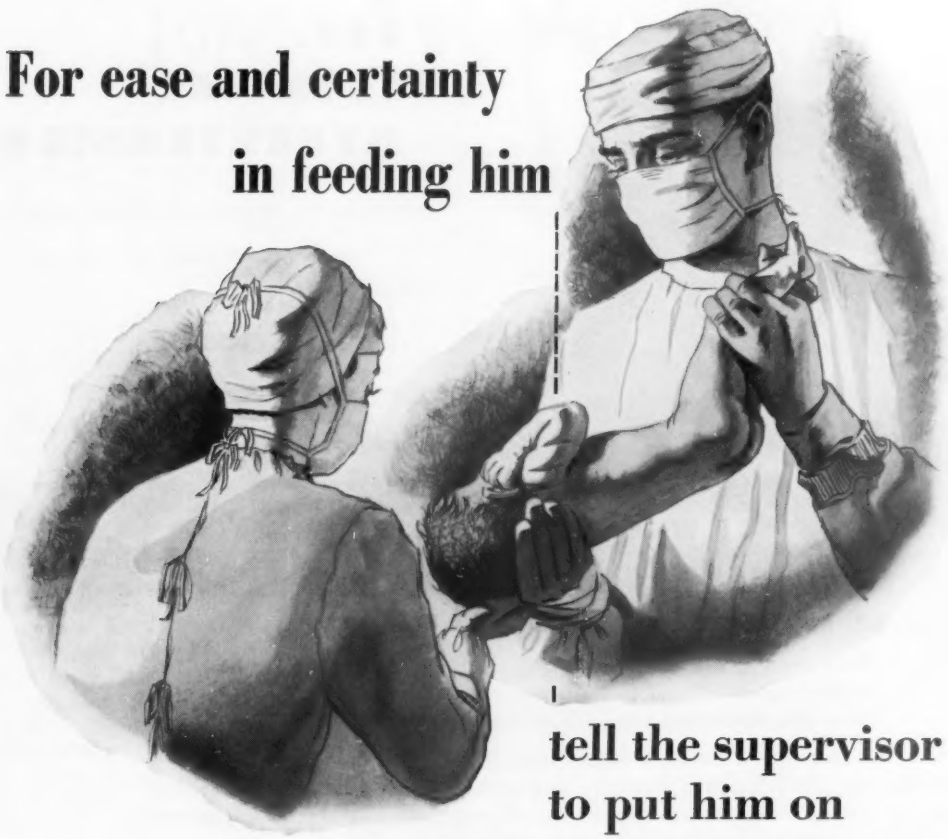

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DRAINAGE OF RIGHT PULMONARY VEIN INTO INFERIOR VENA CAVA*

Report of a Case, with a Radiologic Analysis of the Principal Types of Anomalous Venous Return from the Lung

VICTOR A. MCKUSICK, M.D.,† AND ROBERT N. COOLEY, M.D.‡

BALTIMORE

UNTIL recently anomalous drainage of pulmonary veins into the right side of the circulation (anomalous pulmonary venous return, drainage or connection, with transposition of the pulmonary veins) was considered a most unusual condition and one rarely diagnosed in life. With the more extensive practice of angiocardiography and cardiac catheterization the anomaly has been recognized with increasing frequency. Furthermore, clinical and roentgenologic correlations have indicated that in at least some of these cases this malformation can be identified without recourse to these specialized procedures. Also, the possibility of surgical correction[1,18] has made more purposeful the attempts at an accurate understanding of the anatomic and physiologic aberrations in the living patient.

This paper presents, firstly, a detailed report of a case of one of the more unusual types of anomalous venous return — namely, drainage of a right pulmonary vein into the inferior vena cava — and, secondly, an analysis of the radiologic features of other cases illustrating the principal types of transposed pulmonary veins.

CASE REPORT

M.F.McC.§ (J.H.H. 343439), a Negress born in 1927, was first seen at this hospital during her first pregnancy at the age of 17 years. At that time she was asymptomatic, but routine x-ray examination of the chest revealed a peculiar cardiac configuration, with prominence of the right border interpreted as cardiac displacement. An abnormal shadow in the right-lung field was not noted.

In 1949 the patient was referred for study because of the same unusual and perplexing finding on tuberculosis survey. Again, she was asymptomatic. X-ray examination of the chest (Fig. 1*A*) showed bulging of the right cardiac border and pulmonary-artery segment, a possible decrease in the normal prominence of the left border of the heart and aorta and, in the right-lung field, a sickle-shaped or inverted-comma-shaped shadow with its lower extremity in the region of the right cardiophrenic angle. Angiocardiograms (Fig. 2*A* and *B*) revealed dilatation of the right atrium, ventricle and main pulmonary artery. The left atrium, ventricle and aorta were perhaps smaller than normal. The sickle-shaped shadow in the right-lung field filled at the same time as the veins of the left lung and showed a clear communication with the inferior vena cava at a point just below its entry into the right atrium. Whether this anomalous right pulmonary vein perforated the diaphragm in its course to the vena cava could not be established with certainty. There was a suggestion that the right inferior pulmonary vein emptied normally into the left atrium.

By 1953 the patient, then 26 years old, had passed through 6 normal pregnancies without event. She had become moderately obese and was then having 3 mild symptoms: easy fatigability, mild dyspnea with exertion and cardiac consciousness, interpreted as palpitation, when she lay on her left side.

Cardiac catheterization was performed on January 20, 1953, by Dr. H. T. Bahnson. Hopes of being able to catheterize the anomalous right pulmonary vein (for oxygen-saturation studies) and both pulmonary arteries (for differential peripheral-artery dye-dilution curves) were not realized. A dye-dilution curve obtained after injection of dye into the left main pulmonary artery was normal and specifically gave no evidence of recirculation such as might occur from left pulmonary veins discharging into the right atrium. Pressures on the right side of the circulation were normal. Pulmonary blood flow was elevated to 5.1 liters per square meter of body surface area per minute, but systemic flow could not be calculated from the data obtained.

OTHER CASES

At least 13 other cases of this unusual anomaly have been diagnosed in life,[2-11] and older reports[12,13] describe this finding at autopsy. The oldest patient in the literature is probably the thirty-seven-year-old patient of Arvidsson.[8] This patient had only minimal symptoms. Some of these patients had total pulmonary drainage into the inferior vena cava[12,13] and other complex cardiovascular anomalies. The diagnosis can be made from the conventional chest film by means of the characteristic features: the sickle-shaped or inverted, commalike shadow in the right-lung field, the bulge of the right cardiac border and the inconspicuous left side. In a case reported by Findlay and Maier[9] a similar sickle-shaped shadow communicated with the right atrium.

This anomaly is compatible with long life with little functional disability, and even that is late in onset.

*From the departments of Medicine and Radiology, Johns Hopkins University School of Medicine and Hospital.

†Assistant professor of medicine, Johns Hopkins University School of Medicine; physician, Johns Hopkins Hospital.

‡Professor of radiology, University of Texas School of Medicine, Galveston, Texas; formerly, associate professor of radiology, Johns Hopkins University School of Medicine.

§This patient was referred to us by Dr. M. E. Brailey. The angiocardiograms were made by Dr. E. C. Peirce, II.

Theoretically, however, surgical removal (or extensive disease) of the lung with normal venous drainage might be disastrous in these patients. If it is known that a major and adequate share of the venous return is to the left atrium, the burden on the right side of the heart could doubtlessly be reduced by excision of this was not achieved in the patient described above.

Bronschospirometry has been performed in at least 2 of these patients.[4,8] Since there is every reason to believe that venous blood leaving both lungs has, for practical purposes, the same oxygen saturation (approaching 100 per cent), oxygen uptake is propor-

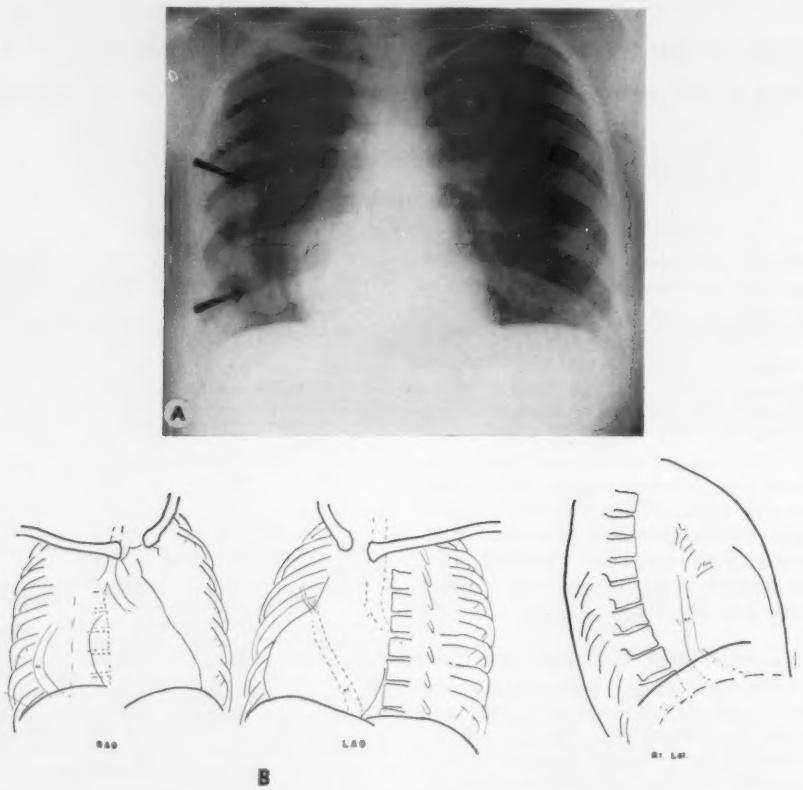

FIGURE 1. *Anomalous Drainage in Case 1.*

A=*an ordinary radiogram of the chest. The comma-shaped shadow in the right-lung field is evident. The bulge of the right border of the heart caused by dilatation of the right atrium and right ventricle is so conspicuous that dextrocardia was the first impression.*

The superior vena cava is probably dilated to a considerable degree.

B=*the course of the anomalous vein as sketched from plain films in the right lateral, right anterior oblique and left anterior oblique projections.*

the lobe or lobes with the anomalous drainage and ligation of the corresponding anomalous veins.[14]

Associated cardiac anomalies were apparently absent in the cases diagnosed during life. The anomalous right pulmonary vein may penetrate the central leaf of the diaphragm and join the inferior vena cava below as in the twenty-year-old soldier on whom Dr. Brian Blades performed thoracotomy.[4]

Differential dye-dilution curves with injections performed separately via a catheter in each of the two main pulmonary arteries should provide good evidence of prolonged circulation time and recirculation in the involved lung. Owing to technical difficulties tional to blood flow in each lung. Analysis of the data of Arvidsson[8] shows that in his patient blood flow through the right lung was 39.5 per cent of total pulmonary flow. After five minutes of exercise this value fell to 33.6 per cent. In spite of these values based on oxygen uptake, minute ventilation was greater in the right lung (3420 cc.) than in the left (2520 cc.). (Although the figures derived can be only very approximate, calculations by means of Arvidsson's data suggest a flow of about 7.6 liters per minute through the left ventricle and one of about 11 liters through the right ventricle.) The other reported bronchospirometric study[4] failed to reveal any abnormality of re-

spiratory function in the lung with anomalous venous drainage. Oxygen uptake and vital capacity were within normal limits.

appears to have been the basis of increasingly severe symptoms and death in the first year or years of life.

The increased minute volume of blood that the

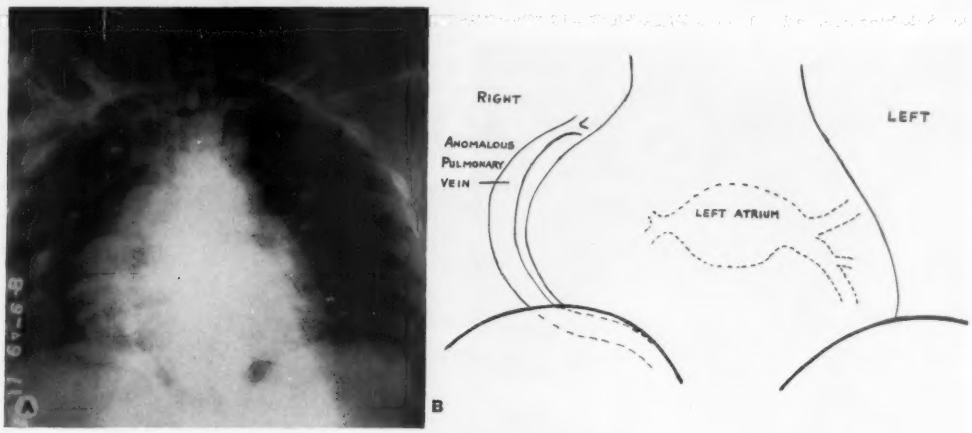

FIGURE 2. *Angiocardiograms in Case 1.*
At this stage (A) *the pulmonary veins are filled. The comma-shaped shadow is seen to communicate with the inferior cavo-atrial junction. Although it cannot be made out in this reproduction but is outlined in the sketch* (B) *the left atrium appears to be abnormally small. Furthermore, it is quite definite that the dye-filled right inferior pulmonary vein enters the left atrium in a normal fashion.*

The angiocardiogram (Fig. 2*A* and *B*) in the case reported above demonstrates very well the diminished size of the left atrium. Furthermore, in cases of total pulmonary venous return to the right atrium the left atrium is even smaller, a feature that makes attempts at venoatrial anastomosis difficult.

HEMODYNAMIC AND OTHER PHYSIOLOGIC CONSIDERATIONS

It is evident that the fundamental hemodynamic abnormality in transposition of the pulmonary veins is the shunting back, to the right side of the circulation, of blood normally destined for the left atrium and the systemic circulation. The hemodynamic abnormality is similar to that of a defect of the interatrial septum and to a lesser extent of one of the interventricular septum. Consequently, there are radiologic similarities arising from these physiologic ones. In partially anomalous venous return with the intact atrial septum, as in the case described above, a significant physiologic difference from defect of the interatrial septum is the anatomic impossibility of even momentary or partial reversal of the direction of the shunt.

As pointed out below in the classification of these cases, there may be either partial or total drainage of venous blood from the lung to the right side of the heart. When there is total transposition there must, of course, be a compensatory intracardiac defect that permits right-to-left shunting. Usually, this defect is interatrial. The patients with total transposition are likely to have at least mild or intermittent cyanosis. If the foramen ovale decreases in size by progressive closure life is threatened. In several of the cases this

right ventricle is required to propel represents an increased work load. The result is hypertrophy of the right ventricle. It must dilate also — that is, its vol-

FIGURE 3. *Plain Film of the Chest Showing a Structure in the Right-Lower-Lung Field That Has the Appearance of a Pulmonary Vein Communicating with the Right Atrium, and Filling of the Anomalous Structure in the Right Lower Lung at the Same Time as the (Other) Pulmonary Veins. The vein appears to discharge into the right atrium and there is recirculation of dye through the right side of the heart.*

ume during diastole must be increased — to accommodate the enlarged stroke volume. The pressure in the pulmonary artery, right ventricle or right atrium is usually within the normal range, except as discussed in the next paragraph. The right atrium also dilates, and the left atrium shrinks to a corresponding degree. The dilatation of the right atrium occurs without measurable increase in atrial pressure; the mechanism of this feature is imperfectly understood.

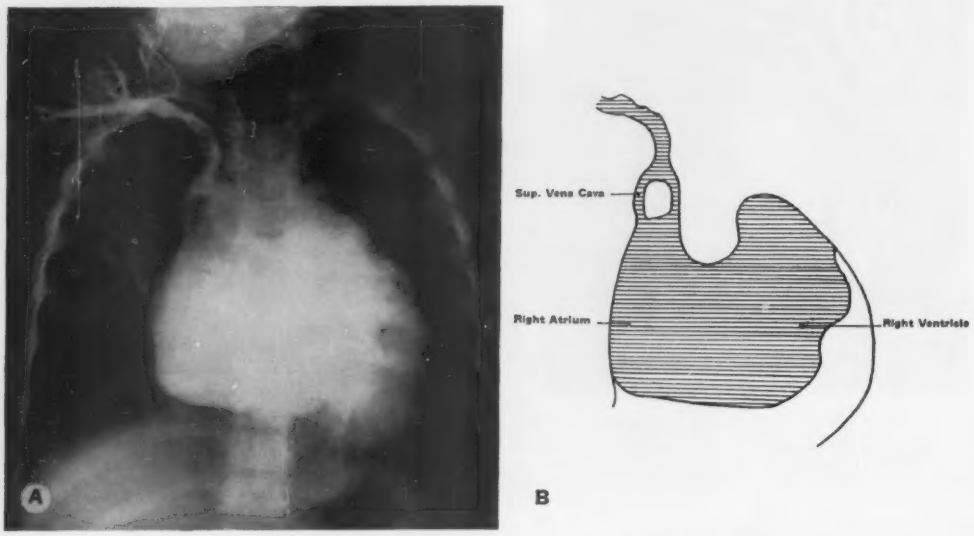

FIGURE 4. *Film from an Angiocardiographic Series Apparently Illustrating Dilution of the Dye and Abrupt Widening of the Vena Cava at the Point Where the Anomalous Pulmonary Vein Joins It.*

Also well demonstrated is the dilatation of the right atrium, right ventricle and pulmonary artery.

TABLE 1. *Types of Anomalous Venous Return.*

TYPE	NO. OF CASES
Partial transposition:	
To inferior vena cava	1
To superior vena cava:	
Right superior pulmonary vein	3
Left superior pulmonary vein	1
To right atrium directly	1
Left pulmonary vein(s) to right atrium via persistent superior vena cava on left & coronary sinus	2
Total transposition:	
To right atrium (unspecified point of entry)	2
To right atrium (via coronary sinus)	1
Figure-of-eight syndrome (persistent superior vena cava on left to superior vena cava on right)	8
To superior vena cava on right via azygos vein	1

On cardiac catheterization several of the cases of anomalous venous return gave evidence of relative pulmonic stenosis — that is, a drop in systolic pressure across the pulmonary valve without anatomic stenosis as shown by subsequent post-mortem examination. The pressure in the pulmonary artery was normal, and that in the right ventricle was elevated. This physiologic finding had its counterpart in the harsh systolic murmur, often accompanied by thrill, at the left sternal border. Presumably, the outflow tract is too small, relatively, to accommodate the increased stroke volume. Another factor in the genesis of both the murmur and the pressure differential is probably the dilatation of the main pulmonary artery, a radiologic feature of all these cases. The same physiologic, physical and radiologic findings occur in defect of the interatrial septum, and a similar pressure drop and systolic murmur occur in congenital dilatation of the pulmonary artery.[15]

True pulmonic stenosis has, of course, been present in some cases of anomalous venous return as well as other anomalies such as patent ductus arteriosus, tetralogy of Fallot and frequently patent interatrial septum. The associated malformation tends to alter the radiologic picture. For example, the association of pulmonary stenosis will reduce pulmonary blood flow and the degree of hypervascularity of the lungs. Partial return of pulmonary venous blood to the right side of the heart must exaggerate the strain imposed on the right ventricle by pulmonic stenosis. However, when there is conspicuous right-to-left-shunt, as with an associated tetralogy of Fallot, the anomalous venous drainage from the lung may be expected to have some ameliorating effect.

With an anomalous drainage involving one lung or a part of one lung only, is blood flow in that portion altered from the proportion of the total pulmonary blood flow that it would normally be expected to receive? Do anatomic, hemodynamic or neurogenic factors alter, in one direction or the other, blood flow in the part of the lung that has anomalous drainage? The pressure in the left atrium is slightly higher than that in the right atrium. Might this not result in a proportional increase in the blood flow in the anomalously drained lung? The only observations bearing on this point[4,8] yielded results that are not in agreement (as evident from the bronchospirometric studies discussed above). These considerations have a bearing on the relative "vascularity of the lung fields" as demonstrated by x-ray examination.

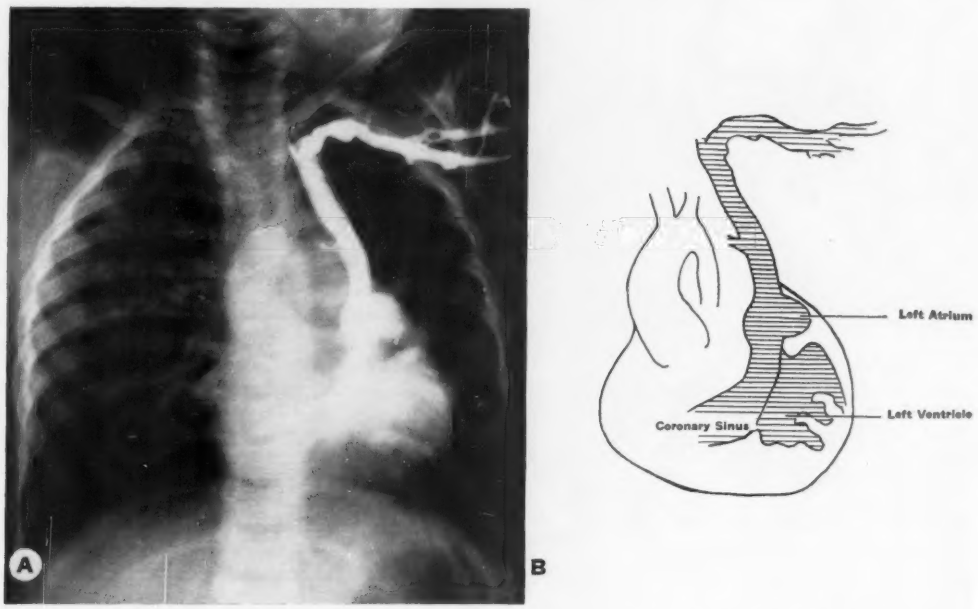

FIGURE 5. *Superior Vena Cava Communicating with an Abnormally Small Left Atrium and with the Right Atrium, Probably via the Coronary Sinus.*

A tributary high on the superior vena cava on the left may be the pulmonary vein, the hemiazygos vein or a communication with the normal right portion. The course of the aorta, which filled early, is normal. The difference in vascularity of the lungs is evident. The small size of the left atrium and the data from cardiac catheterization (maximum oxygen saturation in the right atrium) are consistent with the total transposition of the pulmonary veins. The exact site or avenue of entry into the right atrium has not been established.

GENERAL RÉSUMÉ OF RADIOLOGIC FINDINGS

As in defect of the interatrial septum increased vascularization of the lung fields and "hilar dance" are likely to occur. (This feature may, of course, be absent or reduced if pulmonic stenosis is present as an associated anomaly.) The right atrium is dilated as a rule. The right ventricle becomes dilated and hypertrophied as a result of the increased work involved in the propulsion of the increased minute volume of blood. The superior vena cava may likewise be dilated if it is part of the pathway of anomalous venous return.

Anomalous vascular patterns in the lungs are occasionally detectable, although these changes are considerably more subtle in most cases than the anomalous pattern of drainage into the inferior vena cava illustrated by the case described above. Conventional radiograms of the chest may demonstrate vascular structures that appear to communicate with the superior vena cava or with the right atrium[9] (Fig. 3). There may be a slight outpouching on the silhouette of the superior vena cava at the point where the anomalous pulmonary vein enters (Fig. 4*A* and *B*). In 1 case of drainage of the right upper lobe to the superior vena cava this lobe appeared radiologically to be distinctly more vascular than the rest of the lung. There may be characteristic changes in the upper mediastinum resulting from dilatation of the normal right superior vena cava or from dilatation and characteristic course of a persistent left superior vena cava that receives blood from the lungs.

Angiocardiograms generally reveal the dilatation of the right atrium, right ventricle and pulmonary artery. On the first circulation of the contrast material there is likely to be considerable dilution at the

point in the superior vena cava or in the right atrium where the stream of pulmonary blood joins the systemic venous return. (Dilution in the superior vena cava is not easy to evaluate because the same appearance may be produced by normal admixture of blood from the azygos or innominate vein or both.) The superior vena cava may enlarge abruptly at this point. Recirculation through the right side of the heart or continuous opacification of these chambers can usually be demonstrated. The anomalous veins are often outlined satisfactorily and their drainage demonstrated at the same time in the series when the normal pulmonary veins are filled.

Laminography directed at study of the vascular pattern of the lungs is worthy of further use in these cases. Elucidation of the normal vascular patterns in the lung and of anomalous vascular patterns can be achieved at least in part by this method. Also, in cases of suspected drainage of pulmonary veins into the superior or inferior vena cava, this method properly employed should demonstrate the abnormal communication.

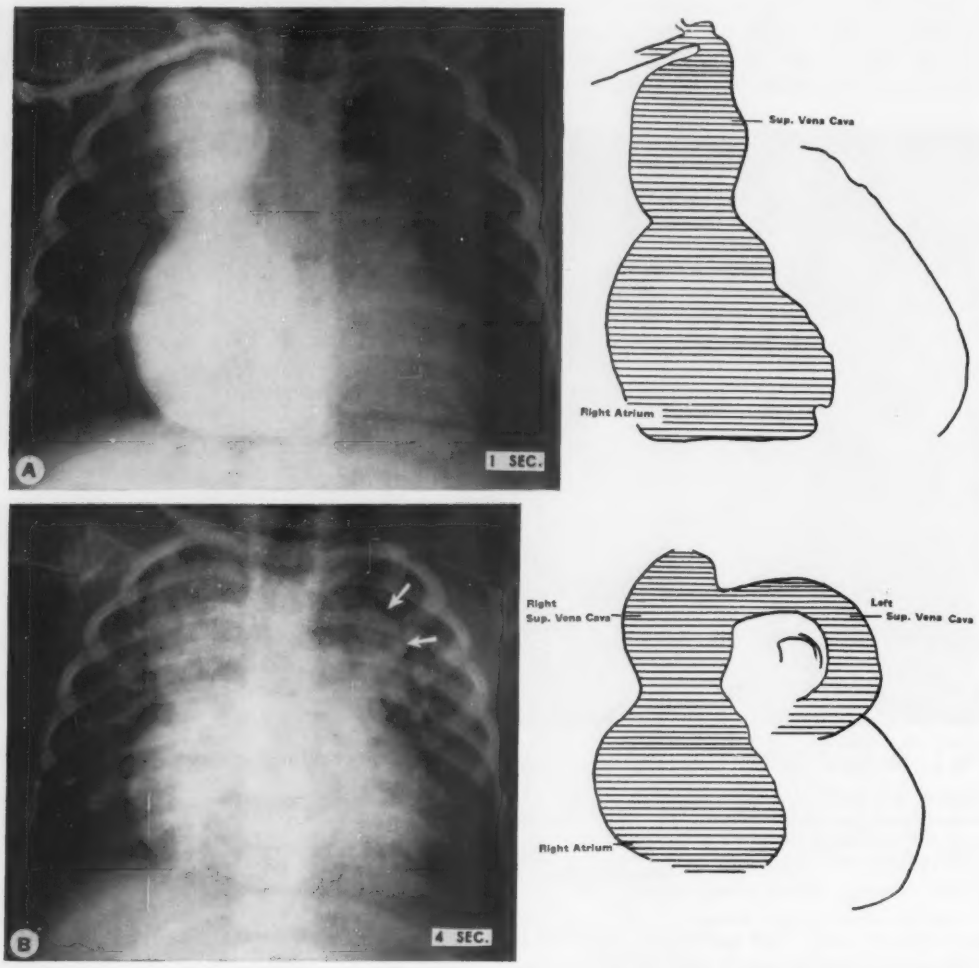

FIGURE 6. *Angiocardiographic Series in a Patient with the Figure-of-Eight Syndrome.*
A *demonstrates the massive dilatation of the right portion of the superior vena cava and the right atrium. The left part of the superior vena cava, better demonstrated on less heavily penetrated ordinary radiograms of the chest, is opacified and the right part and the right atrium are reopacified at the time that the pulmonary veins are demonstrated by the contrast substance* (B).

Classification

Cases representing the types of anomalous venous return shown in Table 1 have been subjected to sufficiently detailed radiologic study to make analysis worth while.

Analysis of Individual Types of Anomalous Drainage

Partial return to superior vena cava. In 4 cases there appeared to be partial return of the pulmonary veins to the superior vena cava. In all but 2 the point of entry of the anomalous veins was in the vicinity of the atriocaval junction. Some would classify these as representing drainage into the right atrium. Trounce[1] has presented a clear angiocardiographic demonstration of anomalous return to the atriocaval junction.

The oldest patient in this group is twenty-four years of age and probably has no other cardiovascular anomaly. The other patients probably have additional cardiac malformations although the exact diagnosis has not been established in several of them.

Figure 4*A* and *B* illustrate two of the radiologic findings in these cases — namely, abrupt enlargement of the vena cava and dilution of the dye at the presumed point of entry of the anomalous vein. (Both findings, of course, must be interpreted with caution since the azygos and left innominate veins enter at about the same point.) Not illustrated (because it could not be reproduced well) is the increased vascularity of the right upper lobe in a patient with tetralogy of Fallot in whom the venous drainage of the lobe was to the normal right superior vena cava.[16] In this case the right upper lobe appeared to be distinctly more vascular than the rest of the right lung, creating a sharp change at the interlobar fissure.

With the exception of 1 case in which the left upper lobe drained into the normal right superior vena cava the drainage was from part or all of the right lung in all the cases of this group.

Partial drainage into right atrium. The veins of the right lung are most frequently involved in this as in the other types of partial transposition. Figure 3 presents the salient radiologic features of 1 of our cases with this particular anomaly. Conventional x-ray examination of the chest revealed an anomalous vascular shadow in the right-lower-lung field that appeared to join the right atrium. That this shadow was due to a pulmonary vein discharging into the right atrium was demonstrated by angiocardiograms.

Left pulmonary veins to right atrium via a persistent superior vena cava on the left and the coronary sinus. In 2 cases the anomaly just described appears to be present. In addition to the less specific manifestations (dilated right atrium and ventricle and pulmonary artery) the conventional roentgenogram of the chest is likely to show a straight-bordered vertical shadow in the upper mediastinum producing widening to the left.

When the contrast substance is injected into the left arm, angiocardiograms show filling of the superior vena cava on the left whereas when the right arm is used the normal superior vena cava on the right is filled. When the left part of the superior vena cava is filled it is apparent that the straight shadow on the left of the upper mediastinum represents this dilated structure. At about the level of the pulmonary-artery bifurcation it arches sharply mediad, producing a hockey-stick configuration. Then, joining the greatly dilated coronary sinus, it discharges into the right atrium through its ostium on the posteroinferior wall. During the first course of the contrast substance through the left part of the superior vena cava, reflux into the tributaries of the pulmonary veins on the left is likely to occur. Reopacification of the superior vena cava occurs at the same time as the pulmonary veins are demonstrated. At this stage communication between the left pulmonary veins and the superior vena cava is usually clearly demonstrated.

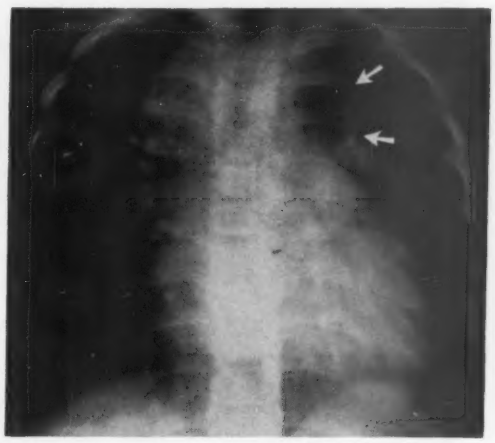

FIGURE 7. *Ordinary Radiogram of the Chest in Another Patient Showing the Typical Figure-of-Eight Configuration. As in Figure 6 the left part of the superior vena cava (arrows) is the least dense component of the anomalous cardiovascular stripe.*

Total drainage of pulmonary veins into right atrium (site and avenue of entry into right atrium not specifically determined). Two cases are of this type. The case illustrated in Figure 5 is an unusual one and probably represents transposition of the veins with total drainage of the pulmonary veins into the right atrium and at least partial systemic drainage into the left atrium. In 1 case all venous drainage, both pulmonary and systemic, was into the right atrium. The congestive heart failure and death at an early age were almost certainly the result of the small size of the interatrial communication. In neither of these cases were radiographic studies, including angiocardiography in the former, of much help as far as the anomalous venous return was concerned.

Total drainage of pulmonary veins into right atrium via coronary sinus. One case was very similar to the latter case of the last section in that both showed globular enlargement of the heart and death in congestive heart failure at an early age owing to partial physiologic closure of the foramen ovale, whose pat-

ency was the only associated abnormality in these cases. The only difference, a minor one, was the demonstration at autopsy that the veins entered the right atrium via the coronary sinus.

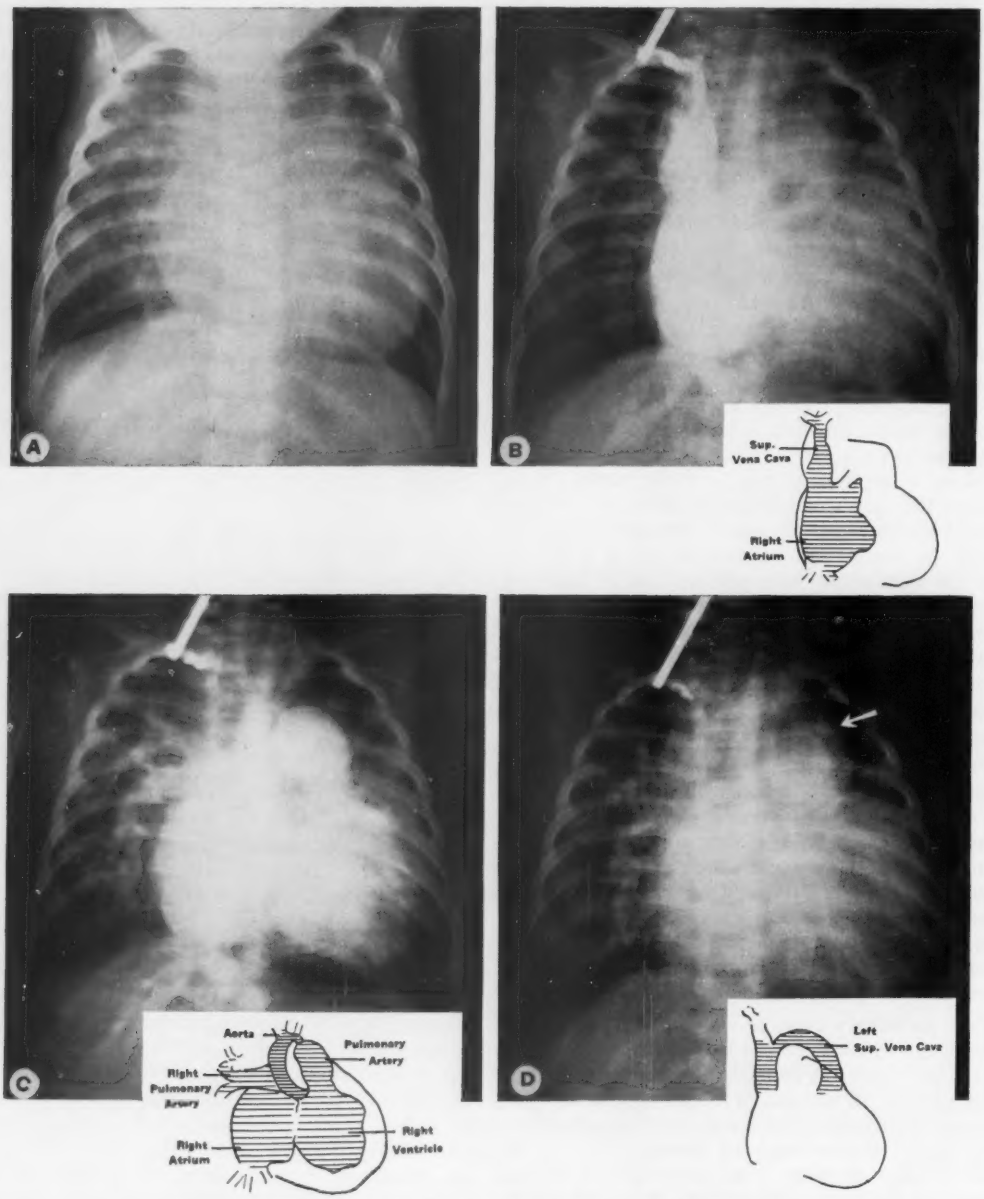

FIGURE 8. *Films in Another Patient with the Figure-of-Eight Syndrome.*
The configuration of the cardiovascular stripe (A) *is fairly typical. There is increased vascularization of the lung fields. The three representative films from the angiocardiographic series* (B, C *and* D) *demonstrate the dilatation of the chambers and vessels on the right side of the circulation as well as the anomalous veins themselves.*

The figure-of-eight syndrome (persistent left to right part of superior vena cava). Eight unequivocal cases of this malformation have been studied at this hospital. This anomaly derives its name from the characteristic silhouette of the cardiovascular stripe. (Fig. 6-9). In this situation all pulmonary veins return to the right side of the heart. The pulmonary veins on the right drain into a transverse venous sinus that lies

behind the upper portion of the left atrium but does not, as a rule, communicate with it. This transverse venous sinus joins a persistent superior vena cava on the left that also receives all the venous return from the left lung. The left portion of the superior vena cava arches around superiorly to join the normal right part, which discharges into the right atrium. (Figure 6 presents a sketch of the characteristic anatomic findings in these cases.) Both portions of the vena cava are dilated, producing a shadow in the upper medi-

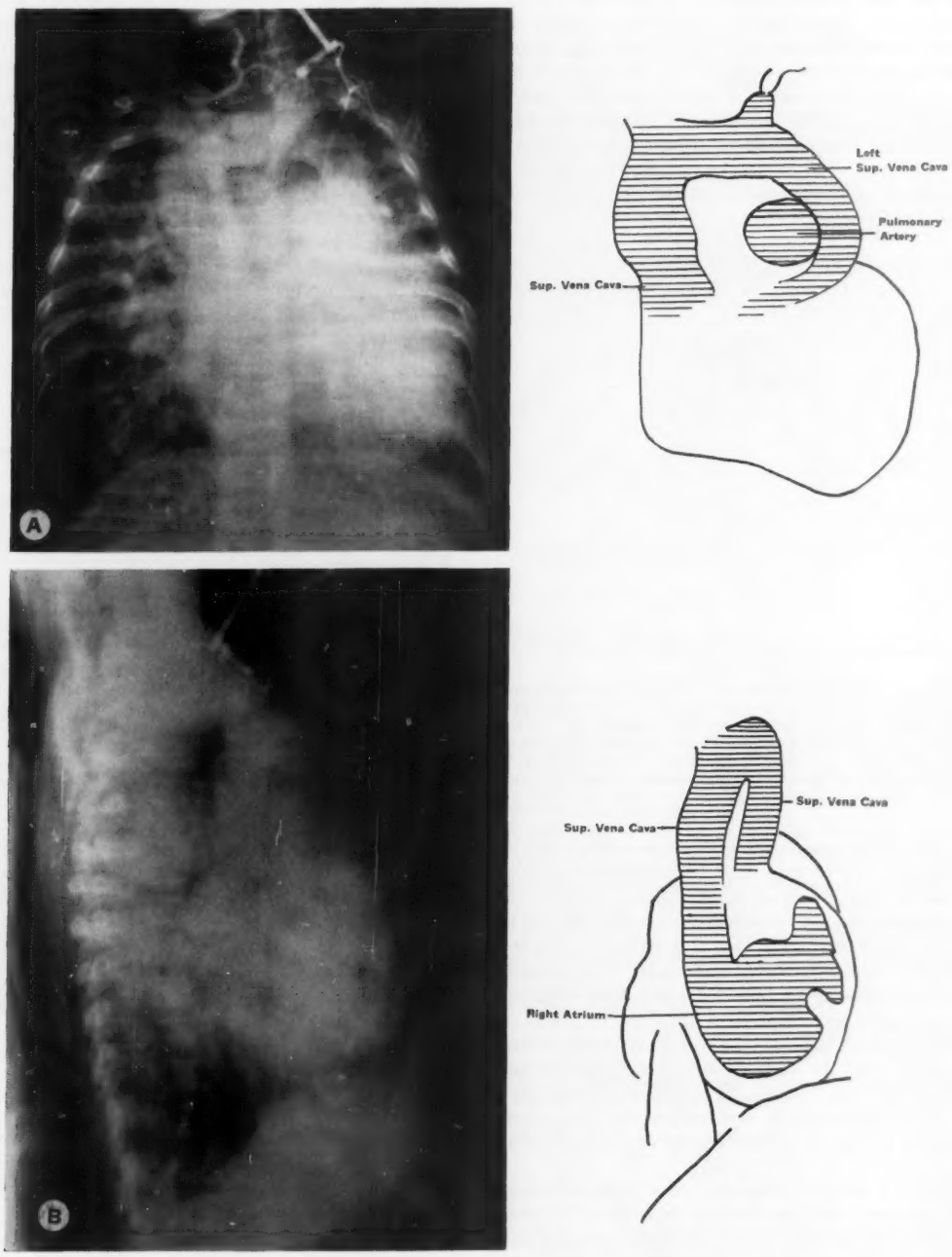

FIGURE 9. *Posteroanterior* (A) *and Lateral* (B) *Views at the Same Time in an Angiocardiographic Series. At this point the pulmonary veins are demonstrated, and the superior loop is opacified. The typical figure-of-eight configuration is clearly demonstrated.*

astinum that is almost as wide as the shadow produced in the lower mediastinum by the heart. In all these cases the only communication with the systemic circulation is via a persistently patent foramen ovale. In several cases physical incapacitation, heart failure and death appeared to be related to the finding at autopsy that the foramen ovale had become partially closed. In many respects the hemodynamic pattern in these cases of total transposition of the pulmonary veins is very similar to that in cor biloculare. One of these cases did, in fact, have a two-chambered heart in association with anomalous pulmonary venous return.

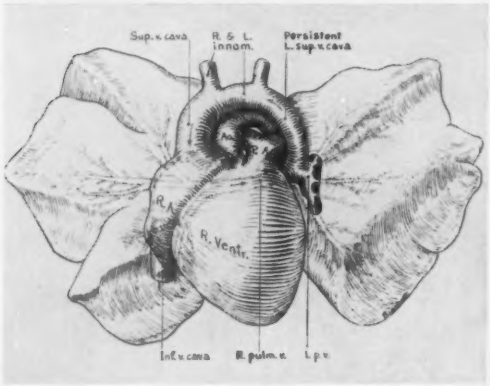

FIGURE 10. *Sketch of an Anatomic Specimen in a Patient (Reproduced from MacManus[17] with the Permission of the Publishers).*

All venous drainage from the right lung is into a transverse venous sinus, which courses posterior to the heart and joins a persistent superior vena cava that receives the venous drainage from the left lung. Obviously, all pulmonary venous return is to the right side of the heart. The genesis of the figure-of-eight configuration of the cardiovascular silhouette is apparent.

Figures 6 to 10 illustrate the pertinent radiologic feature in this group of cases. Fluoroscopy is likely to demonstrate active pulsations of the dilated superior vena cava. In 1 case this pulsation was well demonstrated by roentgenkymograms. The pulsation may have resulted in part from tricuspid regurgitation produced by dilatation of the right ventricle. At operation the heart was likely to be unusually free in the pericardial sac since it lacked its posterior pulmonary-vein attachments. Similarly, on fluoroscopy in the lateral position, the area behind the heart corresponding to the left atrium and its veins might be unusually clear.

This is a situation, like that of a right pulmonary vein emptying into the inferior vena cava, in which the diagnosis can be at least strongly suspected from the conventional roentgenogram of the chest. Except for a patient who died in 1938 and another, one of the youngest of the group, who died before more than ordinary radiography could be performed, the anomaly was diagnosed with certainty during life in all these cases. A mistaken diagnosis of mediastinal lymphoma or of aortic aneurysm has been made in some of these cases.[11]

About 17 other cases of this syndrome have previously been reported,[5,17-28] and others are constantly being added to the literature. One patient in this series (Fig. 11), twenty-eight years of age, is older than any previously discussed. Three patients, 2 twenty-four[28,29] and 1 twenty-two[5] years old, both with relatively little incapacitation, have been mentioned. Recently, a forty-two-year-old patient with the "figure-of-eight" anomaly has been described.[11]

It is likely that satisfactory surgical correction of this anomaly will not be attained until the interatrial defect is closed. Merely re-establishing direct communication of the drainage of the pulmonary veins with the left atrium will probably be of relatively little benefit.

SUMMARY

A case of anomalous return of the pulmonary veins to the inferior vena cava is presented. Radiologic features of 19 other cases, representing eight varieties of anomalous drainage, are presented. In retrospect it appears that a malformation of this type could have been at least suspected from the ordinary radiogram of the chest in 11 of these cases. In 5 additional cases angiocardiography suggested or established the diagnosis.

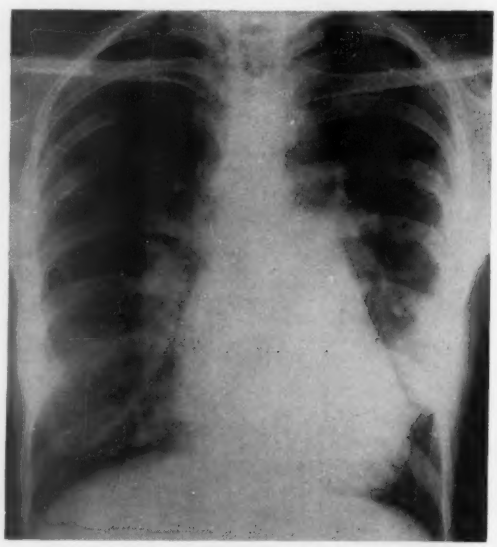

FIGURE 11. *Conventional Radiogram of the Chest in a Twenty-Eight-Year-Old Patient, Showing the Classic Figure-of-Eight Conformation of the Cardiovascular Shadow. Angiocardiograms were equally typical.*

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OBSTRUCTION OF THE RENAL ARTERY PRODUCING MALIGNANT HYPERTENSION

IRVING IMBER, M.D.,* AND ROBERT H. CLYMER, JR., M.D.†

READING, PENNSYLVANIA

ONE of the most important recognized factors in the pathogenesis of hypertension is the role of the kidney. In spite of tremendous effort the mechanism by which hypertension is produced in renal disease has remained obscure. It is our purpose to report a case in which malignant hypertension was caused by an extrinsic compression of the right renal artery and permanently relieved by removal of the right kidney. We consider this case worth adding to those already reported because the arterial obstruction was demonstrated by aortography before operation and because severe functional impairment of the contralateral kidney, which existed at the time of the operation, subsequently cleared completely.

CASE REPORT

A 34-year-old dairy worker was admitted to the Reading Hospital on March 10, 1953, complaining of pain in the head, marked fatigability, loss of appetite, loss of 40 pounds in weight, nausea and vomiting. He had been examined for life insurance 1 year previously, when the blood pressure was reported to be normal. Approximately 1 month before entry his symptoms began with fatigability, loss of appetite and then loss of weight. Just before admission he noted severe occipital headaches and pain radiating into the back of the neck. This pain was accompanied by nausea and occasional vomiting. The family history revealed moderate hypertension in both the mother and the father. A review of the systems was negative.

Physical examination showed a well developed, somewhat thin, apprehensive man. The blood pressure was 195/130 in both arms. Ophthalmoscopic examination revealed Grade 3 Keith–Wagener hypertensive retinopathy. The heart sounds were regular and normal; no murmurs were detectable. The remainder of the examination was well within normal limits. Preoperatively, from March 10 to March 20, the blood pressure varied from 170/110 to 210/150 on numerous examinations.

Examination of the blood disclosed a red-cell count of 5,010,000, with a hemoglobin of 15 gm. per 100 cc., and a white-cell count of 9950, with 76 per cent neutrophils, 1 per cent eosinophils and 23 per cent lymphocytes. Urinalysis revealed a specific gravity of 1.004, a pH of 6.0, a ++++ test for albumin and a negative test for sugar, with 3 or 4 white cells and 3 or 4 red cells per high-power field and many hyaline casts in the sediment. The fasting blood sugar was 62 mg., and the blood urea nitrogen 30 mg. per 100 cc. The electrocardiographic tracing demonstrated simple sinus tachycardia. Repeated urinalyses showed a +++ to ++++ test for albumin, and a repeat examination revealed a blood urea nitrogen of 35 mg. per 100 cc. The maximum specific gravity (Mosenthal concentration test) was 1.013. Benzodioxane administered intravenously caused no change in the blood pressure. The Sodium Amytal sedation test (consisting of 0.2 gm. of the drug at hourly intervals for 3 doses) was performed. At the beginning the blood pressure was 185/130. There was no appreciable change in the readings until the 3d dose, when the blood pressure fell to 170/120 3 hours later.

X-ray examination of the chest was negative.

An intravenous urogram showed very poor function of the right kidney, with no visualization of dye until the 1-hour film (Fig. 1). The left kidney appeared somewhat larger than the right and functioned normally.

The retrograde pyelogram of the right kidney (Fig. 2) appeared morphologically normal, although the right kidney appeared somewhat smaller than usual. The calyxes were not deformed, and the morphology of the renal pelvis was quite normal. On the left side the pyelogram was again normal, but the kidney appeared somewhat enlarged.

*Instructor in medicine, University of Pennsylvania School of Medicine; associate in medicine, Reading Hospital.

†Visiting lecturer in urology, University of Pennsylvania Graduate School of Medicine; associate in urology, Reading Hospital.

An aortogram (Fig. 3) showed a normal left renal artery and normal blood supply to the left kidney. On the right side the renal artery was deformed at the hilus of the kidney, and the lumen appeared constricted in this region. The density of the dye in the proximal portion of the right renal artery was about half that on the left side.

Cystoscopic examination of the bladder demonstrated no abnormalities. The orifice of the right ureter showed almost as active peristalsis as that of the left, but very little urine issued from it. No indigo carmine was excreted from the right side after 20 minutes. On the left side the ureteral orifice excreted indigo carmine after 4 minutes.

FIGURE 1. *Intravenous Urogram, Showing Poor Visualization of the Right Kidney After an Hour.*

Ten days after admission to the hospital nephrectomy was performed on the right. At operation the adrenal gland appeared grossly normal. The renal pedicle was thoroughly explored, and a good many fibrous bands about the renal artery and the renal vein were seen, binding the artery firmly to the vein and having so kinked the artery that it made a complete S turn (Fig. 4). At one of the bends of this S, the artery appeared considerably compressed, and pulsations distal to this point were diminished. The renal artery and renal vein were separated with moderate difficulty owing to the adhesions. No further disease could be demonstrated. The kink in the renal artery could not be entirely freed and had a tendency to recur. There was no gross evidence of active inflammation. The renal artery was not traced behind the vena cava.

One hour after operation the blood pressure was 110/80, and on the evening of operation it fell as low as 98/66. The postoperative course was uneventful, and the blood pressure eventually stabilized about 130/70. By the 8th postoperative day the ophthalmologist reported an improvement in the hypertensive retinopathy. Three days after operation the blood urea nitrogen was 41 mg. per 100 cc. On discharge 8 days after operation there was only a trace of albumin in the urine; the blood urea nitrogen had fallen to 22 mg. per 100 cc.

On pathological examination the kidney measured 11 by 4.5 by 1.8 cm. and weighed 100 gm. The capsule stripped with ease. The cortex was smooth. The cortical-medullary demarcation was well differentiated, the cortex measuring 0.8 cm. and the medullary portion 1.0 cm. The pelvis was slightly distended, with evidence of recent mucosal hemorrhage. The ureter appeared normal. There was a small fibrous band surrounding the renal artery approximately 1 cm. before its bifurcation in the hilus. The lumen was patent and gave no evidence of change in the intima.

The renal structure appeared normal on microscopical examination.

One month after operation the patient still complained of easy fatigability. On ophthalmoscopic examination the fundus was normal. He had gained 20 pounds in weight, and the blood pressure was 132/85. Urinalysis revealed a specific gravity of 1.015, with no albuminuria and rare white cells in the sediment. By June 22 he stated that he felt fine. He had gained another 10 pounds in weight. Ophthalmoscopic examination remained negative. The blood pressure was 135/82. The specific gravity of the urine was 1.021 and no albumin or microscopical abnormalities were noted. By September 14 he had no complaints; the blood pressure was 125/80, and the specific gravity 1.026. On March 20, 1954, the blood pressure was 130/85, and the specific gravity of the urine was 1.030, with a normal sediment. Eighteen months after operation the blood pressure was 120/85. The blood urea nitrogen was 17 mg. per 100 cc., and urea clearance 74 per cent of average normal function (normal for laboratory).

FIGURE 2. *Retrograde Pyelogram Revealing Morphologically Normal Right and Left Kidneys.*

DISCUSSION

The demonstration of a hypertensive state by the Goldblatt technic in laboratory animals has made it mandatory to investigate the kidney status in the young, rapidly progressive hypertensive patient.[1] At present the only adequate means of establishing a causal relation between urologic disease and hypertension in any patient is by "cure" of the hypertension on removal of the offending kidney. Narrowing of one or both renal arteries of sufficient degree to produce malignant hypertension has been recorded.[2]

These cases have usually been due to the intrinsic disease of the artery itself.

Many reports have appeared of unilateral renal lesions in man, with hypertension cured by nephrectomy. Perhaps the first reported case in which no renal disease was present in the kidney was that of a six-year-old boy with a pelvic kidney.[3] This may well have represented vascular insufficiency. Its removal resulted in a permanent cure of the hypertension.

FIGURE 3. *Aortogram, Showing Obstruction of the Right Renal Artery (Arrow) and Normal Filling of the Left Renal Artery and Kidney.*

Rigid criteria for cure have been established by Smith.[4] These consist of pre-existing hypertension of some duration and blood pressure reduced to normal levels by operation and remaining normal for at least a year.

The case presented above met all these criteria. It is not possible to state the exact length of time in which the hypertensive state was present, but it can be assumed to have been at least a month and less than a year before operation. This emphasizes the general contention that good results are achieved most frequently in patients whose hypertension is of recent origin and rapidly progressive to the malignant phase.[5]

It is generally accepted that azotemia, presence of albuminuria and poor concentration of urine reveal grave functional impairment of both kidneys that, in most cases, has been regarded as irreversible and as prohibiting surgical "cure." Fishberg[6] considers nephrectomy justified for hypertension only if function of the diseased kidney is negligible and function of the contralateral side is unimpaired. However, in the case reported above, the functional capacity in the contralateral kidney could not be considered good according to these criteria, and there was at least moderate impairment of total kidney function. Yet a cure of the hypertension and return to normal kidney function were accomplished by removal of the offending kidney. This suggests that a certain degree of reduction of kidney function should not obviate surgery and that the contralaterally diminished renal function is reversible at least to a certain point. The apparent reduction in function of the left kidney and its steady improvement over a year are unique.[7] The low specific gravity could not have been simply the result of hypertension and flood diuresis, for if so there should have been a normal specific gravity as soon as the blood pressure was reduced. The slow recovery of concentrating power and the preoperative elevation in nitrogen are suggestive of tubular impairment.

The problem of the degree of functional impairment necessary for a kidney to produce hypertension is of interest in this case. The intravenous urogram and cystoscopic examination showed marked diminution in dye excretion from the affected kidney, but the presence of some appreciable function in the affected kidney was clearly demonstrated.

In the series of cases reported by Howard and his associates[2] the functional capacity of the contralateral kidney was considered excellent. Thompson and Smithwick,[8] on the basis of biopsy and "cure" after nephrectomy in 2 cases, believed that the presence of significant vascular disease in the remaining kidney was not a contraindication to nephrectomy. Definite pathological changes are generally noted in the kidney producing the hypertension. The kidney in the case reported above, however, was morphologically normal, and the artery gave no evidence of intrinsic disease. The absence of histologic change is perhaps associated with the short duration of the hypertension and may account for the excellent return of function in the remaining kidney. It is in such situations that preoperative biopsy of the kidney may be of some prognostic importance.

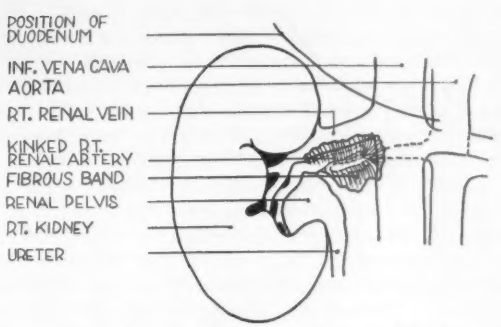

FIGURE 4. *Diagrammatic Representation of a Kinked Renal Artery Beneath a Fibrous Band.*

By disclosing the vascular abnormality in the renal arterial tree, abdominal aortography proves its clinical usefulness in this situation. Howard and his associates[2] reported 2 cases in which this procedure was carried out with similar clinical help. The technic is simple and carries a negligible risk when performed with modern contrast mediums such as Urokon and Neo-Iopax. Series of over 1000 cases have been reported without serious complications.[9] The procedure can be done in any hospital with modern radiologic equipment.

Summary and Conclusions

A case of malignant hypertension due to a fibrous band constricting the renal artery is presented.

Despite bilaterally diminished renal function removal of the offending kidney, which pathological examination showed to be normal, effected a "cure" of the hypertensive state by the most rigid criteria.

The value of abdominal aortography in identifying the vascular defect is again demonstrated.

This case provides further evidence that a diminished blood flow in a major renal artery may cause hypertension and impairment of total renal function.

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MYSOLINE

An Effective Anticonvulsant with Initial Problems of Adjustment

William H. Timberlake, M.D.,* John A. Abbott, M.D.,† and Robert S. Schwab, M.D.‡

BOSTON

THE adequate control of epileptic seizures continues to be a challenge to medicine. Mysoline, an agent effective against several types of seizures, recently became available.[1] More physicians should be aware not only of its range of effectiveness but also of its proper administration and its side effects. If it is not started in small doses so that the body develops tolerance to its side effects, it may have to be prematurely discarded, and the patient deprived of its help.

Mysoline (5-phenyl, 5-ethyl-hexahydropyrimidine-4:6 dione), also called "Primidone," though chemically different, has a structure that resembles that of the barbiturates,[2] as demonstrated by a comparison of its formula with those of phenobarbital and Mebaral (Fig. 1). Perhaps this relation is responsible for its being — like such drugs — effective in several kinds of seizures. It is available in 250-mg. scored, white tablets.

We are reporting our experience since 1952 with Mysoline§ in 96 patients. Most of these patients attended the Epilepsy Clinic of the Massachusetts General Hospital; some were private patients, and a few were treated in the hospital for seizures developing after brain surgery.

The patients' ages have an even but skewed distribution, with the mode in the third decade. The youngest patients were twelve, and the oldest was sixty-nine years of age. They were equally divided between the sexes.

We have classified the seizures into 8 groups: psychomotor automatism, grand mal, focal motor, focal sensory, brief spells, petit mal, other types and not epileptic. When a patient had more than one type of seizure, we have evaluated the effectiveness of Mysoline against each type. Our results — 34 per cent of all spells more than 50 per cent controlled (Table 1) — are comparable to those of others (Table 2).

Method

Most of our patients were already taking one or more anticonvulsants. To avoid precipitating seizures, Mysoline was added gradually, and the previous medication was continued. In some cases one tablet of the other medicine was omitted for each tablet of Mysoline given. In others, as control of seizures improved or as side effects developed, the other medicines were reduced and finally omitted if possible. If the patient became drowsy, the sedative medicine such as phenobarbital or Mesantoin was reduced. If the patient became ataxic and was taking Dilantin, we decreased that.

We recommend starting a patient on Mysoline with half a tablet (125 mg.) a day. If this was given at bedtime, the patient was less apt to be affected by drowsiness, a common transient early side effect. In

*Instructor in neurology, Harvard Medical School, and assistant in neurology, Massachusetts General Hospital (on leave of absence).

†Instructor in neurology, Harvard Medical School; assistant neurologist, Massachusetts General Hospital.

‡Assistant clinical professor of neurology, Harvard Medical School; neurologist and director of Brain Wave Laboratory, Massachusetts General Hospital.

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three to seven days the dose was increased by half a tablet in the morning. In most cases further half-tablet increments were made at similar intervals to allow the body to develop tolerance to the medicine and thus to avoid side effects. In some patients more rapid increases in medicine and even an initial schedule of 3 tablets a day were tolerated without trouble. A few patients had to be regulated even more slowly, and rare patients had an "idiosyncratic" response to even a quarter of a tablet as an initial dose. We have not found any benefit in concentrating the drug into two doses daily instead of three or four doses a day.

Effect on Various Types of Seizure

Thirty-seven patients had psychomotor automatisms. Of these 6 were completely controlled, and 12 had less than half as many seizures. Eight of these improved patients were on Mysoline alone in doses of 250 mg. four times a day to 500 mg. three times a day. In 2 patients automatisms became worse, and 1 patient, whose automatisms improved slightly, began to have grand-mal convulsions instead.

Generalized tonic-clonic, grand-mal convulsions occurred in 36 patients. Twelve of these while taking Mysoline were completely free from spells, 1 for nineteen months. Four received Mysoline alone in doses of 125 mg. twice a day to 250 mg. four times a day. Nine other patients had less than half as many spells. Two patients in status epilepticus were brought under control with Mysoline. One patient with grand-mal seizures became worse on Mysoline alone. One previously mentioned patient with psychomotor automatisms started having grand-mal seizures for the first time as his psychomotor spells improved. None had the prolongation of aura described by Whitty.[12]

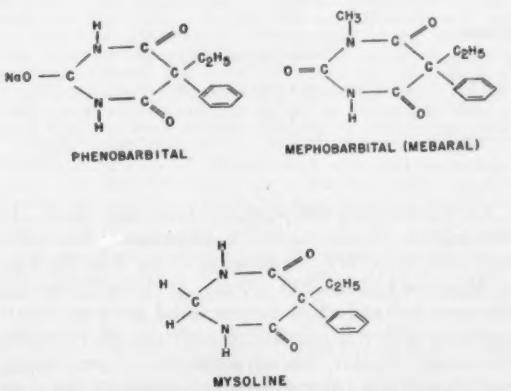

Figure 1. *Structural Formulas of Phenobarbital, Mebaral and Mysoline.*

Focal motor — that is, jacksonian — seizures occurred in 12 patients. One was seizure free on 250 mg. of Mysoline and 100 mg. of Dilantin, both taken twice a day. Three were more than 50 per cent improved, 1 on 250 mg. of Mysoline alone four times a day.

In contrast, none of the 6 patients with focal sensory seizures were more than 25 per cent better even though all were taking anticonvulsants in addition to Mysoline. One was worse.

Brief spells of unwitnessed unconsciousness occurring in patients who had other types of seizures were assumed to be abortive seizures of the usual type rather than petit-mal attacks if the electroencephalogram never contained spike and slow-wave activity. However, since one cannot be certain of the nature of these spells, the 5 patients who had them are considered separately. Only 1 of the 5 was more than 50 per cent better controlled on Mysoline.

Table 1. *Effectiveness of Mysoline in Various Types of Spells.*

Type of Seizure	100 Per Cent Control	50 - 100 Per Cent Control	25 - 50 Per Cent Control	0 - 25 Per Cent Control	Seizure Made Worse	Totals
	No. of cases	No. of cases	No. of cases	No. of cases	No. of cases	
Psychomotor automatism	6	12	6	11	2	37
Grand mal	14	9	1	12	2	38
Focal motor	1	3	2	6	0	12
Focal sensory	0	0	0	5	1	6
Brief spells	0	1	2	2	0	5
Petit mal	1	0	0	1	1	3
Other	0	3	2	10	0	15

Petit-mal episodes — that is, brief lapses without motor activity and with the characteristic spike and slow-wave electroencephalogram between seizures — occurred in only 3 of our patients. On Mysoline, 1 had fewer but more prolonged spells. The second, with grand-mal as well as petit-mal attacks, has not been removed from Milontin, which was already giving complete control of the petit mal. The third was uninfluenced by Mysoline. Our series is too small to settle the discrepancy in the reports of Briggs and Tucker,[4] Butter[5] and Smith and McNaughton[11] of benefit in petit-mal seizures and the reports by Doyle and Livingston[6] and Sciarra et al.[9] of no benefit.

Myoclonic episodes in 3 patients were completely controlled. One patient had Mysoline added to his regular medicine. Two patients were more than 50 per cent better on 125 mg. of Mysoline at bedtime.

Two patients with adversive seizures and a third with movement of the eyes, incontinence and falling improved on Mysoline. In a fourth patient episodes of gagging, nausea and perspiration were more than 50 per cent improved, though his grand-mal attacks were unaffected, when 250 mg. of Mysoline four times a day was added to his 100 mg. of Dilantin taken twice a day.

Bonkalo and Arthurs[3] reported no effect in 8 pa-

tients with episodic psychiatric disorders and temporal-lobe electroencephalographic abnormalities. We found no improvement either in a patient with attacks of aggressiveness but normal electroencephalogram or in a patient with hysterical seizures. One patient with confusional episodes when drinking was not improved by Mysoline.

Side Effects

No side effects occurred in 33 of our patients (34 per cent). In some of these cases the dose of Mysoline was sufficient to control the spells. In other patients, whose spells were not controlled, there were no side effects even though Mysoline was increased to 7 tablets a day alone or 6 a day in addition to 4 Dilantin capsules.

In assessing the side effects among the remainder of our patients one must remember that Mysoline was usually added to the medication that the patient had previously been receiving. In some patients the dose of that drug was reduced as Mysoline was added on a one-for-one basis. In other patients, however, the previous medication was not reduced until the spells were beginning to come under control or side effects that might have been due to additive effects with the other medicine began to appear. Moreover, if spells were not controlled, we generally continued to increase the Mysoline dose until side effects appeared.

Goldin[13] has described a severe reaction to the first dose of Mysoline as "idiosyncrasy." Such reactions occurred after the first dose of Mysoline in 15 of our patients. Three were taking no other medicine, and 1 was taking only 200 mg. of Dilantin a day. The reaction began half an hour to two hours after the first whole or half tablet was taken and might incapacitate the patient for twenty-four to thirty-six hours, with drowsiness, weakness, a feeling of drunkenness, headache, nausea, vomiting and diplopia (1 case). None of these patients had a rash or blood dyscrasia. One patient who reacted thus to half a tablet of Mysoline alone was given a quarter tablet ten days later and had a similarly distressing reaction. However, half a tablet was usually tolerated when repeated later. Case 1 illustrates this. Because the kinds of symptoms are the same as those occurring with overdosage and there is subsequent toleration, this effect is probably an extreme reaction of the cumulative type and not a different type of reaction as implied by the term "idiosyncrasy." Eight of these patients, who refused to continue with further trial of the medicine, are included in the group that was unimproved or "0-25 per cent" controlled (Table 1) so far as the effect of Mysoline on seizures was concerned.

Table 2. *Various Spells Completely Controlled or Markedly Improved in 646 Cases Reported by Other Authors.*

Authors	No. of Patients in Series	Psychomotor Automatisms	Grand-mal Attacks	Focal Motor Attacks	Brief Spells	Petit-mal Attacks	Other Types	Psychiatric Episodes
Bonkalo & Arthurs[3]	18	10 of 10	—	—	—	—	—	0 of 8
Briggs & Tucker[4]	22	—	8 of 9	—	5 of 6	6 of 12	—	—
Butter[5]	58	1 of 1	16 of 58	—	—	—*	—	—
Doyle & Livingston[6]	100	0 of 3	19 of 31	0 of 10	—	0 of 4	—	—
Greenstein & Sapirstein[7]	30	0 of 4	16 of 22	5 of 6	—	1 of 3	—	—
Handley & Stewart[1]	40	29 of 40	—	—	9 of 15	—	—	—
Nathan[8]	21	—	—	—	—	—	9 of 21	—
Sciarra et al.[9]	121	10 of 15	33 of 50	11 of 21	—	0 of 6	6 of 13	—
Smith & Forster[10]	100	6 of 10	34 of 42	—	—	1 of 4	28 of 37	—
Smith & McNaughton[11]	66	8 of 27	5 of 13	1 of 5	—	4 of 13	8 of 17	—
Whitty[12]	70	8 of 13	25 of 29	6 of 7	—	4 of 8	—	—

*23 per cent — number not given.

Drowsiness was the most common side effect. It was mild in 23 and marked in 18 patients. It usually appeared in the first day or so, or by the time the dose of Mysoline had reached 500 mg. It cleared when the dose was reduced. In 1 patient it did not recur when the same dose was reinstituted after two days without the drug. It also cleared when the accompanying barbiturate was reduced without change in the dose of Mysoline.

Weakness was complained of by only 4 patients. In these it constituted a part of the "idiosyncratic" response. It was a generalized feeling.

Sixteen patients complained of dizziness. None described true vertigo. Rather, it seemed that they had a giddiness or lightheadedness. Most of them were among the 21 patients with ataxia.

Nine patients complained of mental dullness. Three of these and 4 others were confused.

Six patients were nauseated, 2 of them to the point of vomiting.

Five patients had throbbing or pounding headaches or a feeling of heaviness and pressure over the eyes. Five patients reported impaired sexual potency, as noted in 1 case by Sciarra et al.[9] Four patients had transient rashes clearing in a day or two when medi-

cine was stopped and not recurring when it was started again.

Three patients became irritable. Two had impairment of memory.

One patient each had blurred vision, narrowed vision, diplopia, euphoria, talkativeness, bad breath, anorexia, enuresis and constipation. Although 1 patient had a slight personality change, none had psychoses such as those described by Briggs and Tucker[4] and Nathan.[8]

Frequent urinalyses gave no indication of renal damage. There was no clinical evidence of liver damage. Briggs and Tucker[4] reported a case of leukopenia, and Case 2 of our series may have had a disturbance of blood formation caused by Mysoline. But repeated blood counts in the other patients showed no dyscrasias.

Since Mysoline produces drowsiness so readily, it is best not to combine it with the barbiturate anticonvulsants during the initial trials, and, in many cases, the barbiturates may not ever be required.

Case Reports

Case 1. R.R., a married, 53-year-old plumber, had no family history of epilepsy and no history of difficulty at birth or head injury. His 1st seizure had occurred at the age of 27. All seizures were associated with sleep, either daytime naps or at night, and were of 2 kinds: generalized convulsions and myoclonic jerks. He had tried Dilantin and, for the past 8 years, had taken phenobarbital, 15 mg. 3 times a day. A month before starting Mysoline he had given up both medicines because they were ineffective. At 9 a.m. he took 1 250-mg. tablet of Mysoline and went for a walk. He felt dizzy while walking and for the rest of the day he slept a good deal. At work the next morning he had "no strength . . . pain in my stomach . . . my mind didn't work right, I couldn't think clearly." He left work early and again slept most of the day. On the 3d day he felt "all swollen up" for the first 3 hours but worked a full day. After this reaction to 1 tablet of Mysoline he returned to Dilantin, 100 mg. twice a day, and phenobarbital, 15 mg. at bedtime. These medicines proved disappointing, and 11 months later he again tried Mysoline. For 4 days he took half a tablet at bedtime. During the 1st 2 days he had a "full head," abdominal cramps and mild diarrhea. He was then free of symptoms and on the 5th day began taking a 2d half tablet of Mysoline in the morning without ill effects. Five months later he was taking half a tablet at breakfast and at supper time and a whole tablet at bedtime. He was free of convulsions, he was no longer irritable, and he was gaining weight. Nocturnal restlessness and the myoclonic jerks persisted but were milder. Despite the initial reaction to Mysoline on 2 occasions a tolerance to the medicine gradually developed, and he was able to take it in amounts sufficient to control his grand-mal convulsions and lessen his myoclonic jerks.

Case 2. K.M., a 28-year-old woman, had a history of petit-mal and generalized convulsions since the age of 12. At the age of 25 there was evidence that some of the seizures were due to a cerebral scar, which was successfully excised. A large number of anticonvulsant medications were tried, with only partial success. In January, 1953, she was placed on Mysoline, starting with 125 mg. once daily until 500 mg. twice daily and 200 mg. of Mebaral at bedtime was reached in 2 weeks. Her spells were controlled. After 6 weeks on this schedule the routine white-cell count had dropped to 3000, with only 50 per cent neutrophils. Both drugs were withdrawn, and the count promptly returned to 6000. Mysoline alone was resumed without leukocyte suppression, nor was there any change in the blood picture on Dilantin and Mebaral. When Mysoline, 500 mg. twice daily, and Mebaral, 200 mg. at bedtime, were taken the white-cell count dropped quickly to 2000, returning to normal when the Mebaral was omitted. In this case an unusual sensitivity of the white cells resulted when 2 drugs were used together, neither of which affected the white-cell count when used alone. At no time was there any subjective or objective evidence of difficulty from these temporary drops in the white-cell count. One year later the count on Mysoline, 500 mg. twice daily, was normal.

Conclusions

Mysoline is an effective anticonvulsant in patients with psychomotor automatisms, grand-mal, focal motor and myoclonic seizures, giving complete to excellent control in 54 per cent.

Its principal side effects are drowsiness and ataxia. Only one patient may have had a disturbance of blood formation due to Mysoline combined with Mebaral. No kidney or liver damage was encountered.

By starting with half a tablet of Mysoline at bedtime and very gradually increasing the dose, tolerance can be built up in the body, and side effects can be minimized. Infrequently, a severe reaction may follow even a small initial dose. However, this may not recur later, and the patient may go on to tolerate doses effective in controlling his spells.

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MEDICAL PROGRESS

SYPHILIS*

ROBERT F. TILLEY, M.D.†

BROOKLINE, MASSACHUSETTS

FIVE years have elapsed since the last progress report on syphilis appeared in this journal. During this period the value of penicillin has been established not only in early infectious syphilis but also in late symptomatic syphilis. The worth of the broad-spectrum antibiotics has been demonstrated. The treponema-immobilization test shows great promise in eliminating false-positive reactions from true or syphilitic reactors. Seldom has a single serologic procedure been accepted so enthusiastically. Long-term observations have delineated the course of both treated and untreated patients. The World Health Organization has undertaken the conduct of mass campaigns against venereal and nonvenereal treponemal diseases. In the United States the management of syphilis has changed from the public-health physician to the family physician; the ease, short duration and nontoxic qualities of penicillin therapy instituted this shift. This factor, together with a decrease in incidence, has created a falsely optimistic view that syphilis has been eradicated. Marked curtailment in public funds has caused a restriction in much needed venereal-disease control activities. This five-year period has also seen the end of the *Journal of Venereal Disease Information* and the *Journal of Syphilis, Gonorrhea and Venereal Diseases*. The former was combined with several other publications and appears in *Public Health Reports*. Publication of the latter has been abandoned.

PUBLIC HEALTH

Control of syphilis by public-health measures has been possible since the discovery of the *Treponema pallidum* in 1905.[1] According to data obtained from military sources there has been a steady decline in new cases in Western Europe and the United States since valid statistics were first compiled in 1865. This decrease has been attributed to the natural change of the host-parasite relation, to improvement in socioeconomic conditions and finally to relative population stability after periods of instability. All these factors continued to be operative after 1910, and there has been an accelerated drop in incidence. Mortality has declined more rapidly than morbidity. These results have been produced by the effective treatment of millions of persons and by programs designed to bring people to treatment.

Many public-health administrators have expressed the optimistic outlook in stating that present scientific knowledge will effect control and eventual eradication of syphilis. The final effect of penicillin cannot be measured for another ten years. The present decline is not yet sufficient to promise complete control. Thus, control efforts must not be relaxed. The component parts of a control program include items whose effectiveness is difficult to assay. The elevation of socioeconomic status with improvement in general education and recreational opportunity is of questionable value. Specific education concerning the dangers of venereal disease is effective but relatively expensive. Repression of prostitution has a definite place, but punitive measures are useless and harmful. The available prophylactic measures, including the use of penicillin, have been of limited value in military life and of less help in civilian society. Steady progress has been made in improving methods of diagnosis and therapy. Improved serodiagnostic facilities and employment of mass surveys have helped locate hitherto unreached population groups. Penicillin has replaced the more dangerous drugs. It has the advantage of being rapid, safe and cheap. It produces a cure rate of 80 to 85 per cent in early syphilis, and all patients complete the necessary course of therapy. The disadvantages of penicillin are the increased chance of infectious relapse and the greater prevalence of reinfection; these may occur in 10 per cent of those treated.

The hope for complete and global control of syphilis awaits basic studies dealing with *T. pallidum*, its culture and the eventual development of some type of immunization.[2] No disease has ever been eradicated by treatment of infected persons.

An analysis of the results of federal control of venereal disease shows that in the eleven years that these measures have been in effect (from 1938) great strides have been made. The 1951 infant mortality rate was a fifth that of 1938. The general mortality rate from syphilis has been reduced. Admissions to mental hospitals because of syphilis have been reduced 34 per cent. There has been a constant decrease in morbidity.[3] Despite these remarkable results control is still a major problem, since in 1949 there were 150,000 newly infected persons (80,000 of these undiscovered), 6000 persons admitted to mental institutions for the first time because of syphilis, 14,000 infants with the diagnosis of congenital syphilis, 13,000 deaths attributed to syphilis and an estimated 2,000,000 people in the United States with positive serologic tests. During this eleven-year period federal, state and local governments have spent $315,628,768 in

*From the Department of Dermatology and Syphilology, Harvard Medical School and Massachusetts General Hospital.

†Assistant in dermatology, Harvard Medical School; assistant dermatologist, Massachusetts General Hospital.

administering the public-health measures that have helped attain these results.[4] The savings effected by the reduction in mental admissions have exceeded this sum. Over 14,000 more infants would have died from congenital syphilis during the period 1936 through 1948 if the death rate for 1933 had continued. A premature reduction in available federal funds for venereal-disease control has been deplored since complete control is not now in sight and since more active measures are needed.[5] A decision to reduce funds from $9,800,000 allotted in 1953 to $5,000,000 in 1954 and $2,300,000 in 1955 is premature. It is hoped that $10,000,000 will be made the annual budget until a thorough study of the program is presented to Congress for evaluation. The Government should then reduce the budget selectively and gradually.

With the advent of penicillin therapy there has been a change in the place and manner of treatment.[6] No longer need the patient seek help at a clinic or in a hospital. The private physician now administers the therapy, which is a simple procedure, rapid and nontoxic. The experienced syphilologist is fast losing his experience and is only being used occasionally as a consultant. With this change in management the individual physician assumes the responsibilities not only of diagnosing and treating but also of obtaining the necessary data for contact tracing. Trained personnel should be available from the local health department to supplement this important phase of managing the individual patient.

At present premarital laws are in effect in 40 states and in the territories of Hawaii and Alaska. These laws vary a great deal and augment other legislation pertaining to venereal-disease control. To be effective they must be properly enforced.[7] The value of the premarital law is in discovering unknown infections. A recent study in California has shown that, in the twelve-year period from 1937 through 1951, 2,156,678 persons were examined, and of these there were 8106 patients with untreated syphilis and in addition 2977 who needed further therapy.[8] The cost of this program for the entire period has been $10,523,253, or, stated in another way, it has cost $1298 to discover each undiagnosed case of syphilis.

Another use of the serologic test has been in the mass survey of certain groups suspected of having a high rate of syphilis. Since there are an estimated 2,100,000 persons who have syphilis the value of such surveys is great. This was borne out in the investigation of a group consisting of industrial employees in North Carolina.[9] The majority were unskilled laborers and were Negroes. During the three-month study 1244 persons were tested. Excluding the usual false-positive reactions a total of 182 were found to be syphilitic, and of these 96 needed treatment. Late cardiovascular or central-nervous-system disease was found in 17.

Global Measures

International groups have always been interested in the control of nonvenereal treponemal disease such as yaws, bejel and pinta, and in 1949 WHO established a committee to study the group including syphilis.[10] The practical advantages of an over-all unitarian concept of the treponemal diseases is based on the many things that these diseases have in common. It is hoped that by means of mass diagnostic surveys and treatment of infected persons these diseases will be eradicated.[11] The efforts of this group in two years have been prodigious. They have examined 4,000,000 people and have treated 1,000,000 cases of yaws, syphilis and bejel. Follow-up studies, including serologic surveys as late as thirty months after treatment, have been very satisfactory.

The incidence of all types of syphilis reported in Massachusetts has shown a steady decline.[12] In 1936 a total of 5450 cases of all types was reported, 2025 in 1949, and 1775 in 1953. Greater reductions in incidence of infectious syphilis have been noted, with less than 200 cases reported in 1953. Congenital syphilis has all but vanished.

Thus, it can be said that although the complete eradication of syphilis and the other treponemal diseases is not immediately at hand, continued, forceful efforts on local, state, federal and global levels will eventually complete the task.

Experimental Studies

The failure to grow pathogenic strains of *T. pallidum* on artificial culture mediums still plagues the research worker. Ignorance still exists regarding the chemistry, growth requirements and life cycle of the organism. More knowledge about immunity, allergy and tissue predilections is needed, and a serologic test for syphilis must be developed. All these unknown factors must be dispelled before possible mass-immunization procedures can be made available.

Detailed observations on several different nonpathogenic strains of *T. pallidum* cultured on various artificial mediums were compared with those seen in the pathogenic *T. pallidum* from experimental rabbit syphilomas.[13] By means of the phase-contrast microscope it was possible to observe similar stages of development in all the organisms. Transverse fission was seen as the most frequently occurring method of vegetative reproduction. Another was the formation of dense granules along the bodies of the spirochetes. These became buds or gemmae, which elongated and thus formed daughter spirochetes. Multispirochetal cysts formed on clusters of organisms, and from them spirochetal filaments developed, mature and subsequently separate, and emerged as adult spirochetes. These unusual reproductive methods tend to place spirochetes in a distinct group separated from bacteria and protozoa. Other observations utilizing the

various nonpathogenic strains have led to the conclusion that the *T. pallidum* and related organisms can be regarded as pleomorphic organisms whose morphology is determined to a great extent by their environment.[14] Variations in length occur at times of most rapid multiplication, ring forms result from exposure to harmful agents, and round bodies arise as a result of osmotic imbalances or other stresses found in slide cultures. Granules are found regularly. Budding develops at the ends, on the sides or within the cytoplasm. There is no evidence available as yet that makes the hypothesis of a true life cycle a necessary conclusion.

Immunity

The understanding of the immune mechanisms operative in human and experimental syphilis still escapes the clinician and investigator. Repeated injections of spirochetes of the Reiter strain failed to protect rabbits from later syphilitic infection.[15] No immunization developed, but there was a prolonged incubation period and smaller lesions were seen. This observation suggests that the Reiter strain of spirochetes and *T. pallidum* are antigenically related. No increase in immunity was noted, after successive cured infections, over the immunity produced by the initial infection in rabbits.[16] A single untreated infection was shown to be responsible for more immunity than that established by repeated infections of short duration. Multiplication of the organisms was curtailed by the original infection, and this in turn was possibly followed by a reduction in the amount of antigens and thus less immunity. Another possible explanation is that the immunity may be due to more profound tissue response to infection. These results and the theoretical consideration partially explain the failures to date with various efforts to perfect vaccine technics.

During subcurative therapy more immunity develops in laboratory animals than is seen in untreated infections.[17] This is difficult to interpret as far as human syphilis is concerned, but the data suggest that older heavy-metal therapy, since it was prolonged, permitted more acquired immunity to develop. It is also impossible to determine if this factor or others are responsible for the observed increase in reinfection in patients treated intensively with the more rapidly curative penicillin. Again, these studies bring to mind the often repeated suggestion — one never followed, to my knowledge — that syphilis should not be treated in its early stages.

A purified suspension was prepared from a rabbit syphiloma infected with the Nichols strain of *T. pallidum* and injected intradermally into selected human subjects.[18] No reactions were obtained in 6 normal persons, and none of these had any sign of syphilitic infection as a result of the injection. Three persons with gummas and 8 of 9 with congenital syphilis gave tuberculin-type reactions. Six persons with secondary syphilis were nonreactors. The number of persons with neurosyphilis was too small to be significant. The specificity of this testing material has not been established since the series is not large enough, but it seems that in test injections of patients with destructive lesions a tuberculin type of allergy develops.

Infectivity of Blood

Treponemes have been recovered from the blood stream after inoculation in man and rabbit, during the primary and secondary stages and coincident with early relapse. There has been little confirmatory evidence that infection can be transmitted by blood during latency. Congenital syphilis is thought to result from transient reinvasion of the blood and subsequent penetration of the placental barrier. In a group of 42 rabbits on a high-cholesterol ration the blood of 19 was found to be infectious on transfer to normal rabbits one hundred and fifty-four to nine hundred and thirty days after inoculation.[19] Four animals were infectious on transfer even though they were serologically negative. An attempt was made to determine if the reinvasion of the blood stream by the treponemes was cyclic, but this could not be determined. These observations may explain the development of infectious relapse and the birth of infants with congenital syphilis to mothers thought to be in a latent stage of infection. Perhaps the treponemes are released periodically from some focus.

New Drugs

Several more antibiotics have been employed in the treatment of various stages of syphilis. A total of 79 patients with primary and secondary syphilis were treated with chloramphenicol.[20] The drug, in a dosage of 20 to 30 mg. per kilogram of body weight, was administered for four to eight days. The most effective dose was the larger given for eight days. Fifteen days of treatment was recommended for the management of neurosyphilis. The follow-up periods were short, but the clinical and serologic progress was satisfactory. Poor patient co-operation has been noted whenever oral antibiotic therapy has been attempted, and in its place intramuscular injection of chloramphenicol has been recommended.[21] In a series of 63 patients with a minimum of three months' follow-up study the results were encouraging. Another group treated with chloramphenicol, chlortetracycline or oxytetracycline has been observed for two to four years.[22] It was concluded that these drugs were efficacious in penicillin-sensitive patients but only if the patients could be closely supervised during the course of treatment and in the necessary follow-up periods. A larger series of 101 patients treated with chlortetracycline for early syphilis received 70 gm. in eleven and a half days.[23] After a follow-up analysis of twelve to fifteen months there were 76.7 per cent successes, 21.1 per cent failures and 2.1 per cent reinfections. Twenty-one patients with neurosyphilis were given chlortetracycline by mouth (60-gm. total dose, 2 to 4 gm. per day) and followed for one hundred and

twenty-two to five hundred and seventy-three days.[24] The results were equivalent to those seen after penicillin therapy.

With the advent of the adrenal steroids investigators have been interested in their effect in syphilis. In experimental syphilis cortisone altered lesions grossly, microscopically and chemically.[25] There was an increase in extent of involvement and in the number of *T. pallidum*. With removal of the drug there was a further increase in size, number and character of the pathologic changes. Since there was a greater amount of hyaluronic acid it was believed that the changes were due to an inhibition in the removal of this acid. Other studies have shown that ACTH had no effect on the natural course of experimental syphilis.[26] Prolonged therapy with high doses was followed by diminished inflammatory reaction, and the reparative processes were impaired. There was no change in the number of treponemes and no change in the character of the Jarisch–Herxheimer reaction.

In human syphilis ACTH had no effect in diminishing the symptoms in 5 patients with tabes dorsalis.[27] Cortisone successfully controlled the allergic reactions in a patient known to be sensitive to penicillin.[28] No deleterious effects were noted.

Serodiagnosis

Since the advent of cardiolipin antigen serologists the world over have concerned themselves mainly with the establishment of satisfactory standard methods for the serodiagnosis of syphilis. WHO has established a separate committee to study this problem and thus to develop a "simple, practical, serological screening test for ambulatory testing which is sufficiently sensitive, specific and reliable for the diagnosis of treponemal disease in field programmes."[29] As yet this ambitious goal has not been attained.

Great progress in the serodiagnosis of syphilis has followed the introduction of the treponema-immobilization test. This procedure has utilized for the first time in decades a specific antigen — namely, treponemes obtained from a rabbit syphiloma. Although still a cumbersome, sensitive reaction restricted to a few research laboratories the procedure has demonstrated its tremendous worth. Its universal use and practical application rest on the ability of the serologist to make it simple and reproducible for the average technician's ability. Not only is the test of value in diagnosis but also it holds promise of revealing some of the unknown aspects of the immunology of syphilis. The technic is complex and difficult, with many factors that can go astray. Basically, the patient's serum is incubated for forty-eight hours with complement and a suspension of treponemes from a rabbit syphiloma. The positive reaction is based on the number of treponemes immobilized. Time, temperature, dilutions of the various solutions and the number and vitality of treponemes are subject to great range of error. Finally, the reading of the test is based on the experience or lack of experience of the observer.

Serums and cerebrospinal fluids from patients with various types of untreated syphilis were examined for the immobilization factor.[30] All serums after the primary stage were strongly positive. The cerebrospinal fluid was also positive in neurosyphilis as well as in some cases of late syphilis in which the routine serologic tests were negative. Further extensive studies over a two-year period dealt with 455 patients known to have syphilis on the basis of clinical findings or the demonstration of treponemes in their lesions.[31] The immobilization test was found to be highly accurate. In primary syphilis it may be negative. A positive reaction may become negative if adequate therapy is given in early syphilis. Frequently, the test remains positive although the routine serologic test may convert to negative. In this situation a positive immobilization test does not indicate need for further treatment.

At the outset the specificity of the immobilization procedure was acclaimed, and its practical application in the study of the so-called false-positive reactor sought. The standard serologic test utilizes a nonspecific antigen to determine the presence of an antibody in human serum. This antigen, known as reagin, is found in the serums of man and animal. It exists in trace amounts in normal serum, in larger amounts in normal serum in 1 out of 5000 and in increased amounts in human patients after some nontreponemal diseases and in all treponemal diseases. The presence of the antigen in all but the last is known as a biologic false-positive test. The frequency of such reactors has never been determined, but it is believed that as many as 50 per cent of those giving a positive reaction in a mass survey are probably false-positive reactors.[32] Approximately 24 abnormal conditions are capable of producing a false-positive test, and the majority of these diseases are of infectious origin. The acute reaction disappears in six months or less, but the chronic persists for years and even for an entire life.

By means of the treponema-immobilization test it is possible to separate the true reactor from the false, since the reaction is positive in almost all phases of syphilis except the very early primary stage and those treated very early in the course of their infection. This test remains positive almost certainly for the duration of life except when treatment is started early. A normal person never has a positive immobilization test. In a series of 300 subjects with chronic false-positive reactions the test was negative in 43 per cent in whom a diagnosis of latent syphilis would ordinarily have been made. The determination that the individual patient does not have latent syphilis only partially relieves the clinician since a large proportion of these persons later have a serious problem such as one of the collagen diseases. Another study emphasizes the value of the immobilization procedure in determining the false-positive reactor and again emphasizes the fact that acute disseminated lupus erythematosus is a frequent cause.[33] These authors have also demon-

strated that the test is positive in nonsyphilitic infants and persists for six months whereas reagin usually disappears before three months. In a study of over 1000 patients French serologists concluded that the immobilization test was a valuable one but stated that it was a peculiarly delicate biologic reaction that must be interpreted by competent clinicians and further that it must be the subject of patient research before being taken into general use.[34]

In experimental syphilis the presence of a positive immobilization test was not accompanied by any increase in immunity.[35] Thus, the antibody, like reagin, does not confer immunity.

The problem of seroresistance has been the subject of study in recent years. The mechanism behind this condition is not known. Many who are now managing syphilis for the first time become disturbed when the blood tests are repeatedly positive after adequate therapy and after the lapse of many years. It is difficult for some physicians to avoid further penicillin treatments since the drug is easily administered and is relatively harmless. Further treatment and the lapse of more time generally have little influence on the fixed or seroresistant case. If there is no evidence of active disease clinically a single adequate course of penicillin suffices. Irreparable harm to the patient is done each time the therapist unwittingly advises unnecessary treatment. In many infectious diseases positive specific laboratory evidence of past infection persists. The positive serologic test may persist if the infection has been untreated for a prolonged period.[36] As the untreated infection progresses into the various stages the probability of seroresistance increases. This is also true in untreated congenital syphilis since patients treated before six months of age will usually have negative blood tests whereas those treated after two years of age will usually develop seroresistance.

(To be concluded)

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MEDICAL INTELLIGENCE

BY THE LONDON POST

Wear out or Rust out? — Dental Care — Medical Aspects of Boxing

JOHN LISTER, M.D.

LONDON, ENGLAND

THE National Insurance Act has given every working man the right to a small pension at the age of sixty-five. It has recently been suggested that there are grounds for encouraging a policy whereby people should remain at work longer rather than claim their insurance pensions as soon as they may. The needs of the present-day labor force and the observation of Dr. J. H. Sheldon that "occupation is the best medicine for the aged" are the two main reasons for this view.

The report of a recent investigation into the reasons for retiring or continuing at work throws new light on the present position. At the 1951 census 1 man in 5 over the age of seventy was still at work, and between the ages of sixty-five and sixty-nine half the men were still working. Of those who had retired half had done so on grounds of chronic ill-health, and more than a quarter had retired because of the presence of fixed age limits for employment or of provision for superannuation. Thus, 11 per cent of working-class men reaching the age of sixty-five are compelled to retire by their employers, although three quarters of them would prefer to remain at work. Furthermore, workers in many trades and occupations are eligible for employment pensions in addition to their pension rights under the National Insurance Act. The rate of retirement is twice as great at minimum age among men covered by such schemes as among men in trades not covered by such schemes.

Commenting on these figures, the *British Medical Journal* has pointed out two significant facts. In the first place there are many elderly men who have been forcibly retired who would be willing to take up suitable employment if it were available. Secondly, the medical profession has been taking the responsibility for advising many persons to retire on grounds of ill-health. In the light of Dr. Sheldon's remark that occupation is the best medicine for the aged, it questions whether this is always good advice.

The whole subject presents many problems. Although there is full employment in industry it is often difficult to find suitable work for the disabled, especially when a request is made for part-time employment. Nevertheless, Sheldon stresses the fact that the community has so far taken no advantage of the increased span of life given to humanity by medical science and has actually reacted in the reverse direction by a general reduction in the period during which men are still allowed to be and to feel of use.

Certainly, the increasing numbers of elderly persons in the community is a problem that continues to exercise the minds of planning authorities. In particular they are conscious of the ever-increasing economic burden of large numbers of old people who have become a charge on the State either because they are sick and require medical care or because they are in need of care that no one else will provide. It is surely among the latter group that the preservation of the patient's independence and self-respect is the most important factor. It is these people who are most in need of the opportunity of pursuing some form of gainful occupation within the limits of their capabilities. By means of such employment they will retain their individuality and so avoid becoming a charge on the rest of the community.

* * *

Dentistry is one branch of medical science in which the principle of preventive hygiene has now become generally accepted and practiced. Before the last war it seems that less than 1 adult in 10 went annually to the dentist for treatment of any sort. In 1953 this rate of attendance was exceeded by adults of all ages under fifty-five, rising to 1 in 5 in persons thirty to thirty-four years of age and 1 in 4 in persons ten years younger. The high standard of dentistry that was provided in the armed forces during World War II was one of the factors that awakened public interest in regular dental care. Then, in 1948, the National Health Service offered free dental treatment and the provision of free dental appliances for all in need of them. It was no wonder that in the early days of the National Health Service the demands made by the public were immense. At first it was chiefly the middle aged and elderly who used the service. In 1950-1951 the national dental account amounted to £37,910,000, and of that total £23,750,000 went in dentures alone, whereas only £3,310,000 went to the dental care of children and young persons under twenty-one. By 1953 the national bill had fallen to £18,870,000, with £4,470,000 for dentures, and many more young people were receiving dental treatment. This shift of the emphasis in dental work has largely been attributed to the introduction of part payment or cost sharing by adult patients. In particular there was an immediate reduction in the demand for dentures when a charge for their supply was introduced in 1951. In persons over sixty-five years of age this cut in demand amounted to seventy-five per cent. At the same time there was a similar but less pronounced reduction in the number of dental extractions.

At the time of the introduction of the National

Health Service there must have been a backlog of unsatisfied demands for dentures, but there was a great tendency for those already in possession of dentures to see whether the newly provided free appliances would be better. Furthermore, there was no incentive to take proper care of them, and it was easier to replace damaged dental plates than to repair them.

Children and adolescents, for whom the service is still free, have now become, together with young adults, the chief users of the dental service, primarily for conservative work. Thus, the National Health Service seems to have induced a lasting change in popular behavior and it has encouraged the practice of regular dental inspections as a prophylactic measure.

It has shown, furthermore, that it is a failing of human nature not to appreciate fully anything that appears to be "free." The introduction of deterrent charges into other branches of the National Health Service may be the only way to control the continually rising cost of the service, which may eventually threaten it with ruin.

* * *

Public opinion in this country is sharply divided on the merits of boxing as a sport. The main point at issue is that boxing is unique among the sports of civilized communities in that the object of the boxer is not only to hurt his opponent but, if possible, to render him unconscious. In general, the period of unconsciousness after a blow on the head in the ring is short, and most boxers regain consciousness by the time ten has been counted. On the other hand, it is well recognized that the knockout may have serious sequelae, and although fractures of the skull, posttraumatic epilepsy and the "punch-drunk" state are excessively rare in amateur boxing, they are more likely to occur among professionals. The recent death of a young professional boxer in London after an operation for intracranial hemorrhage caused considerable concern. Furthermore, in a recent article in the *British Medical Journal,* Blonstein and Clarke reported that in the last seven years there have been 6 boxing deaths among amateurs and that all were due to intracranial hemorrhage. These authors believe, however, that amateur boxing can be rendered tolerably safe by adequate medical supervision. The London Amateur Boxing Association insists on a full medical examination of any boy offering himself for membership in one of its affiliated clubs, and great emphasis is placed on the importance of matching contestants in accordance with age, as well as with weight. At the ringside, the referee has the power to stop a bout if a boy receives a bad cut or is obviously outclassed. Bandaging of the hands and the wearing of a resilient mouthpiece are encouraged, and the "sorbo-rubber" floor has been approved.

With these precautions and the presence of a medical officer at all contests, Blonstein and Clarke claim that amateur boxing is a useful and justifiable sport. They consider it to offer the youth a healthy form of physical training and to teach discipline and self-control. In some cases it may be a suitable outlet for psychopathic traits and may help combat juvenile delinquency. Nevertheless, if boxing is to remain high in public esteem, it seems essential that the authorities controlling both amateur and professional contests should act on the recommendations of their medical advisers to minimize the risks of brain injury.

CASE RECORDS
OF THE
MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 41081

PRESENTATION OF CASE

First admission. A twenty-eight-year-old para 2, gravida 2 entered the hospital because of generalized aches and pain associated with low-grade fever of three or four weeks' duration.

The patient had been generally well until five months before admission, when she and her sons, aged four and a half years and eleven months, had an attack of fever, weakness and cough. Her physician treated her with injections of penicillin twice a week, a sulfonamide and chlortetracycline. The temperature fell temporarily, but she had an attack of chills, fever and pain over the anterior part of the chest associated with cough and whitish sputum as well as aching in the muscles of the legs that was absent on arising and worse on standing or walking. At the same time a throbbing headache, relieved by aspirin, and crampy abdominal pain associated with defecation developed. The headache and pains in the legs continued after the fever subsided. Two months before admission she had a fever, with temperatures of 99 to 100°F., that subsided after an eight-day course of penicillin. An x-ray film of the chest was reported as normal. A month later the fever recurred, with a temperature to 99.4°F. When she was seen in the clinic, physical examination revealed no lymphadenopathy or splenomegaly. Cervicitis was treated with cauterization. A smear of the peripheral blood showed 15 per cent eosinophils, and heterophil-antibody agglutination and trichinosis tests were negative. The sedimentation rate was elevated to 24 mm. per hour. At that time her older son was in the hospital with a temperature of 105°F. and tonsillitis, but the other child was well. Her appetite was normal, and there was no known weight loss. She gave no history of having consumed raw fish, beef, pork or milk.

The past history was unremarkable. She had had a tonsillectomy at the age of seven. She had been born in Boston of Italian parents.

Physical examination revealed a well developed, moderately thin, olive-skinned woman who did not appear acutely ill. There were a few small, shotty, slightly tender posterior cervical, axillary and inguinal lymph nodes. There were several carious teeth. The chest was clear, and the heart sounds were of good quality, with regular rhythm without murmurs. The abdomen was flat, and no organs or masses were palpated. There was no evidence of muscle atrophy or tenderness. Neurologic examination was within normal limits, but deep tendon reflexes were hypoactive.

The temperature was 99°F., the pulse 80, and the respirations 20. The blood pressure was 120 systolic, 60 diastolic.

Urinalysis revealed a specific gravity of 1.006 and 2 to 4 white cells per high-power field in the sediment. Examination of the blood showed a hemoglobin of 13.0 gm. per 100 cc. and a white-cell count of 12,500, with 43 per cent neutrophils, 34 per cent lymphocytes, 2 per cent monocytes, 20 per cent eosinophils and 1 per cent basophils. The red cells were normal on smear. The sedimentation rate was 0.70 mm. per minute corrected. The prothrombin time was normal. Tests for febrile agglutinins were negative. A stool was guaiac negative; no parasites were found in it. X-ray films of the chest, lumbosacral spine and thoracic spine were within normal limits. A biopsy of the gastrocnemius muscle was reported as normal. The patient was discharged on the fifth day, with the diagnosis of eosinophilia, cause undetermined.

Second admission (seven months later). In the interim she had continued to have generalized muscular aches and pain, low-grade fever, easy fatigability and malaise. She was able to do her own housework, with benefit from Empirin. She was admitted for a re-evaluation of her illness. Her son also continued having occasional pains and had an eosinophilia (count of 8 per cent) just before his mother's second admission.

Physical examination revealed a chronically ill woman with the same small axillary, cervical and inguinal lymph nodes. A Grade 1, soft, apical systolic murmur was noted. There were also some red, scaly, raised areas on the fingers, palm and interphalangeal spaces. Minimal muscle tenderness was present.

The temperature was 99°F., the pulse 84, and the respirations 18. The blood pressure was 120 systolic, 80 diastolic.

Urinalyses were within normal limits, with specific gravities of 1.003 and 1.013. Examination of the blood disclosed a white-cell count of 14,000, with 50 per cent neutrophils, 25 per cent lymphocytes, 10 per cent monocytes, 15 per cent eosinophils and 2 per cent basophils, and a hemoglobin of 12.0 gm. per 100 cc.; the corrected sedimentation rate was 0.63 mm. per minute. The total protein was 6.34 gm. per 100 cc., with an albumin-globulin ratio of 2.6, and a bromsul-

falein test showed 2 per cent retention of the dye in forty-five minutes. Three blood cultures gave no growth. X-ray films demonstrated a normal chest and carious teeth.

In the hospital the patient continued to have a low-grade fever, with a temperature up to 100°F., that did not respond to crysticillin therapy. The aches and pains were not relieved by aspirin or bed rest. A psychiatrist believed that she did not have a hysterical personality, but was more likely to have a psychosomatic disease. One carious molar was extracted. She was again discharged with the diagnosis of eosinophilia, cause undetermined.

FIGURE 1. *Intravenous Pyelogram.*
There is evidence of pressure on the lateral aspect of the left renal infundibulum, with some spreading of these structures (arrows).

Third admission (two years and ten months later). She continued to have aches and pain, with a low-grade fever, and was followed intermittently in the medical clinic. She had had a normal pregnancy and delivery, six months previously, except that she became quite tired with markedly easy fatigability during the third trimester of pregnancy. After delivery an increase in muscular aches and pains and stiffness of the knees developed. Two weeks before admission severe, gripping pain in the lower abdomen appeared, persisting in varying intensity until admission. The menstrual period was a week late and scanty in amount, without change in abdominal pain. A week before admission she had severe, steady left-upper-quadrant soreness, tenderness and fullness, which increased in intensity. The pain was steady and made worse by moving and deep breathing but was not pleuritic. There was no vomiting or diarrhea but slight nausea and constipation. There was increasing malaise, fever and chills until admission. During the week before admission she received chlortetracycline for two and a half days and an injection of penicillin the night before admission.

Physical examination revealed an apprehensive, thin woman complaining of left-upper-quadrant pain. No murmurs were heard. The liver edge was felt 1 fingerbreadth below the right costal margin on inspiration. The spleen, which was palpable 2 fingerbreadths below the left costal margin, was very tender. There was spasm of the left upper quadrant. A Grade 2 to 3 systolic murmur could be heard over the upper abdomen only.

Urinalysis showed a specific gravity of 1.028 and 3 or 4 white cells per high-power field in the sediment. Examination of the blood revealed a white-cell count of 15,400, with 68 per cent neutrophils, 26 per cent lymphocytes, 3 per cent monocytes and 7 per cent eosinophils, and a hemoglobin of 10.8 gm. per 100 cc. The total protein was 6.4 gm., with an albumin-globulin ratio of 2.2, the bilirubin 0.4 mg., the fasting blood sugar 82 mg., the nonprotein nitrogen 20 mg., and the alkaline phosphatase 6.9 units per 100 cc. The prothrombin time was 38 per cent, and cephalin flocculation was negative in twenty-four and forty-eight hours. Widal, heterophil-antibody and brucella agglutinations were negative, as was a preparation for L.E. cells. An electrocardiogram was not diagnostic of any abnormality. X-ray films of the chest and abdomen were unremarkable, but the spleen could not be seen clearly and the splenic flexure was thought to be slightly displaced medially. An intravenous pyelogram was reported as showing normal renal outlines without any hydronephrosis or hydroureter, but the middle group of calyxes in the left kidney gave the appearance of being compressed from a lateral direction (Fig. 1). The spleen was enlarged.

Six blood cultures and urine culture were reported as disclosing "no growth." Sternal-marrow, pectoral-muscle and axillary-lymph-node biopsies revealed no abnormalities. On the tenth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. ALFRED KRANES*: Did the patient live in Boston all her life?

DR. BENJAMIN CASTLEMAN: She had always lived in Boston.

DR. KRANES: Did she have a fever during the first admission? I assume that she did, since that was why she was admitted.

DR. CASTLEMAN: Here is the temperature chart.

DR. KRANES: The chart shows that during the first admission she had no fever. The highest temperature was recorded as 100°F., by rectum.

*Physician, Massachusetts General Hospital.

This is an interesting and challenging case, and I have serious doubts whether I can find a satisfactory solution. One of the reasons for my uncertainty is the fact that I cannot be sure whether the three-and-a-half-year history that preceded the final admission had anything to do with the events leading to the operation. The fever, the left-sided abdominal pain and the enlarged spleen may have been due to a recent episode, such as acute left-upper-quadrant sepsis, but if that was so I shall have to refrain from speculating about what it may have been. I should prefer to believe that the long history preceding the final admission was relevant; if it was not, two thirds of the protocol has been wasted on irrelevant material, and the history of the previous illness would be the most colossal "red herring" that we have had here.

Assuming then that all this is of importance, I shall go back to the original illness, which started as an ordinary respiratory infection except that it was more severe and prolonged. Nothing was said about the duration or height of the fever in the early part of the illness. One gets the impression that the fever lasted for a number of weeks, so that at first I wondered if this was a primary atypical pneumonia. Since the weeks and months went by with persistence of symptoms and fever, such a diagnosis seems unlikely. On examination here five months after the illness began, there was a slight leukocytosis, an eosinophilia (count of 15 to 20 per cent) and an elevated sedimentation rate. One naturally wonders, since several members of the family seem to have been affected at about the same time, whether this was a case of trichinosis. Such an onset would not be unusual for this disease because severe infestations of trichinella are often associated with pulmonary symptoms, and this woman had a great deal of cough. But it lasted too long. Trichinosis is generally an acute illness that may last for a number of weeks but hardly for months as this one did. The negative skin test also casts doubt on that diagnosis. Negative muscle biopsies are not too infrequent in trichinosis.

Because of the eosinophilia one also wonders about infection with other parasites. There are not many that we encounter in this part of the world. Occasionally, patients with ascariasis have a striking eosinophilia. I recall at least 1 patient who had pulmonary symptoms with ascariasis, the worms migrating up the esophagus and down the trachea, producing pulmonary symptoms. The negative stool examination tends to make that somewhat unlikely. Amebiasis may produce an eosinophilia but not often to this degree. The patient under discussion had no gastrointestinal symptoms, but they may have been modified by the antibiotics, particularly chlortetracycline. I cannot, therefore, exclude amebiasis. One also wonders about echinococcal infestation, but in this part of the world, and in native-born people, it is very uncommon.

The nonparasitic diseases that are capable of producing an eosinophilia must also be considered. Hodgkin's disease, usually resulting in a more moderate eosinophilia, is a distinct possibility, but we lack proof. Polyarteritis nodosa must also be considered. Perhaps my consideration stems from the fact that when I was given this case to discuss I was in the midst of an article on polyarteritis nodosa. It could cause much of what went on — the muscle pain, the abdominal pain, the low-grade fever and the eosinophilia. Some of the features of the disease were not present: there was no renal involvement, hematuria or hypertension. It certainly cannot be excluded. At this stage one would also have to consider the possibility of rheumatoid arthritis, which may also cause an eosinophilia.

During the second admission no information was added except for skin lesions on the hands. I do not know what to make of those; nothing further was said about them. One now learns for the first, — and the last, — time that the patient's son had an eosinophil count of 8 per cent. What weight to put on that is uncertain. It brings up the possibility of familial eosinophilia, but that is a benign disease producing no symptoms and is usually stumbled on accidentally. It is, in most reported cases, transmitted from the maternal side of the family. However, Dr. Castleman will not be able to establish that diagnosis pathologically.

The persistent eosinophilia raises anew the question of some sort of parasitic infestation. Additional stool examinations during the second admission might have cast some light on this possibility. There is no record of any in the protocol. By this time trichinosis can be excluded because of the duration. Hodgkin's disease, polyarteritis and rheumatoid arthritis are still not excluded.

During the final admission, the picture changed a great deal. The patient was much sicker and, I assume, had a much higher temperature although nowhere was the temperature mentioned. We are told that she had chills and fever. I should like to know whether these were real chills.

I am intrigued by the murmur in the upper abdomen. I assume that no murmurs were heard over the heart but that the Grade 3 systolic murmur was heard over the upper part of the abdomen. Is that correct?

DR. CASTLEMAN: Someone heard an apical Grade 2 systolic murmur over the heart during the last admission.

DR. KRANES: Apparently, that finding is of little significance then. I should like to look at the x-ray films, Dr. Hanelin.

DR. JOSEPH HANELIN: I have the films of the last admission only, which show normal-appearing lung fields. In the films from the pyelogram the kidneys are of similar size, and both function well (Fig. 1). The renal margins are well defined superiorly and medially, but it is difficult to make out the lateral margin of either kidney. The lower pole of the left kidney is displaced downward a bit from its usual

position — that is, the left kidney lies somewhat lower than the right. The spleen is slightly increased in size. I think the right kidney is normal in function and morphology. On the left there is evidence of pressure on the lateral aspect of the renal pelvis and calyxes.

DR. KRANES: This looks different from what I had expected.

DR. HANELIN: There is a suggestion of spreading of the major infundibula.

DR. KRANES: As if there were some sort of mass pressing on the kidney?

DR. HANELIN: This could result from either an intrinsic or extrinsic mass; there is definite evidence of pressure on the kidney. That is a finding that persists in two different pyelographic examinations.

DR. KRANES: The x-ray films indicate a mass either in or around the left kidney. If there had been a mass in the retroperitoneal region, how could it be explained on the basis of the various possibilities that I have mentioned so far? Most of them, with the exception of rheumatoid arthritis, could explain this finding if one were willing to stretch a point here and there. Hodgkin's disease could have involved the retroperitoneal lymph nodes, causing the deformity of the renal pelvis. The enlargement of the spleen could readily be explained, but the extreme tenderness could not, unless it was the result of an acute infarction or hemorrhage of the spleen. By this time one looks less favorably on polyarteritis because of the duration of the illness. It was now three and a half years since the patient had become sick, and although polyarteritis may go on for that long, and occasionally longer, it does not do so as a rule. How would one explain the x-ray findings on that basis? One would have to assume that they were due to hemorrhage around the kidney, an occasional site for bleeding from the aneurysms that frequently occur in this disease. If one assumes that this patient had polyarteritis, one has to assume also that the fever, pain and x-ray findings were due to a retroperitoneal hemorrhage, around the left kidney.

Could some parasitic infestation explain this? Until the final illness I had not considered the possibility of echinococcal disease very seriously, but after fever and a mass in the left flank developed one has to consider it more seriously. The great drawback to such a diagnosis is that she was native born and had never left New England. Yet we know that echinococcal disease is occasionally found in native-born persons. One case of echinococcal disease of bone was discussed here two years ago.* I recall a report from Louisiana in which 10 out of 15 cases occurred in native-born persons. Yesterday I called the Angell Memorial Hospital and asked whether adult echinococcal worms or larvae had been encountered in autopsies on dogs. None had been found, I was told. Although it seems unlikely, therefore, one cannot rule it out. I should have thought enough about it in this case to have done a skin test.

I assume that the operation was an exploratory operation for a diagnosis. Under the circumstances it seems like the only reasonable thing to do. I too should have turned this patient over to the surgeons, but before doing so I should have done a skin test for echinococcus. If it had been positive, that would have been my diagnosis; if it had been negative, I should find it hard to choose any diagnosis that satisfied me. Since I have to make a diagnosis, I shall put lymphoma as the most likely one.

DR. EARLE M. CHAPMAN: I admire the skill with which Dr. Kranes, like a desperate man, has sought cover by throwing up a cloud of diagnostic possibilities, including most of the esoteric conditions in the textbooks.

DR. KRANES: This looks to me like an esoteric case.

DR. CHAPMAN: To get back to the ordinary variety of medicine, Dr. Kranes did not consider two possibilities that occurred to me after seeing the films — that is, that there may have been some mischief in the middle of the kidney like ordinary tuberculosis. I looked carefully, but no tuberculin test was done. The other possibility is tumor in the left kidney.

DR. KRANES: You would assume, then, that this finding had nothing to do with the three-and-a-half-year history. I was reluctant to accept that. I grant that it is a distinct possibility, but I was hoping that the whole story would fit together into one pattern.

DR. CHAPMAN: It is indeed a difficult problem; I think this reaches the all-time high in these exercises. The leading complaint in the last entry was steady, severe left-upper-quadrant soreness, fullness and pain. The findings in the abdomen on x-ray examination sound definite. I think we ought to pin Dr. Hanelin down. There must have been an expanding lesion in the kidney area from his description of the deformity of the calyxes.

DR. HANELIN: I cannot commit myself since I am familiar with this case. I was unable to make an etiologic diagnosis when I was confronted with the films, although there was manifest calyceal distortion on the left.

DR. CASTLEMAN: The official radiologic interpretation was "Probable expanding lesion in the left kidney."

DR. JACOB LERMAN: You mentioned amebiasis, and then you did not consider it.

DR. KRANES: I meant to consider it. If the symptoms had pointed to the upper abdomen, to the liver, I should have considered it more seriously.

DR. CHAPMAN: Would you consider a low-grade septic focus in the region — not lymphoma or not tuberculosis, but low-grade infection in an avascular area?

DR. KRANES: Producing an eosinophil count of 15 to 20 per cent? It would fit with one of 3, 4 or 5 per cent but not one of that magnitude.

*Case Records of the Massachusetts General Hospital (Case 38091). *New Eng. J. Med.* **246**:341-345, 1952.

Clinical Diagnosis

Tumor of kidney.

Dr. Alfred Kranes's Diagnosis

Malignant lymphoma involving left kidney and retroperitoneum.

Anatomical Diagnoses

Perinephric abscess.
Pyelonephritis, acute and chronic, with abscess formation.

Pathological Discussion

Dr. Castleman: When the patient was operated on the surgeon found a large mass in the left upper quadrant, bounded by the kidney on one side and the spleen on the other. The splenic flexure of the colon, the tail of the pancreas and everything in between was bound down into one huge mass. The preoperative diagnosis was tumor of the kidney, so when he saw this mass binding the organs together, he thought that he should remove it en bloc rather than try to separate it from the various organs. If it was a tumor and one that had gone on for four years, as the symptoms suggested, it was certainly slowly growing and removing it en bloc would be the only chance of curing the patient.

A dissection of the huge specimen revealed that, except for the kidney, the other organs — spleen, splenic flexure of the colon, adrenal gland and tail of pancreas — were normal. They were all adherent to a hard, fibrous mass of tissue that was either a part of the kidney or attached to it. Further dissection disclosed that even the kidney appeared relatively uninvolved except for a few spots of recent infection. Most of the kidney, especially the superior and lateral portions, was encased in a brawny, tough fibrous-tissue shell 3 to 5 cm. thick in which were chronic abscesses. We could not see tumor anywhere, and microscopical sections showed only subacute and chronic inflammation. In other words this shell represented chronically infected perirenal fascia and fat. One might ask if this had been going on for four years. I think it had. This process can be called a perinephric abscess or perinephritis. This almost certainly developed from a previous cortical abscess of the kidney, although the infection that we see now in the kidney was more recent. Cultures of this showed a pure culture of *Staphylococcus aureus*. I assume there was a low-grade chronic staphylococcal perinephritis that had been present for some years.

Dr. Lawrence Kunz: About 10 blood cultures done during the last week were negative.

Dr. Marian W. Ropes: Are the symptoms gone?

Dr. Castleman: Ten days after operation a pocket of pus was drained from the wound. The patient left the hospital three weeks later, and when she was seen in the clinic about three weeks later the wound was healed.

I am unable to explain the eosinophilia. The count was only 7 per cent just before operation. Postoperatively, it came down to 4 per cent. It will be interesting to follow her to see whether the eosinophilia disappears.

I might say that I had asked Dr. Berg to discuss this case first and asked Dr. Kranes after Dr. Berg reported that he was familiar with the case.

Dr. Robert L. Berg: I was grinning with relief that I did not have to discuss it, especially in view of the "eosinophilic herring." The duration of the case reminds me of a nurse who for three and a half years had comparable complaints of poorly localized abdominal pain, fever, a few white cells in the urine and occasional bacilluria. As the progression of antibiotics developed from 1943 to 1947, the bacterial population changed from *Escherichia coli* to streptococci to pyocyaneus. Three years after onset a perinephric abscess was drained, although at the time of exploration it had not been suspected. She had to be drained a second time for relief.

Dr. Castleman: I believe that 20 to 25 per cent of cases of perinephric abscess are not associated with pyuria; they can be walled off.

Dr. Kranes: Can it be true that during all this period the patient never had any symptoms referable to that area?

Dr. Castleman: Apparently, she did not complain of any.

Dr. Hanelin: Ordinarily, we do not have any difficulty in demonstrating a perinephric abscess; certainly, in its acute form we can ordinarily see obliteration of the normal perinephric fat outline. In this particular chronic case there is actually an increase in the amount of fat in the fibrous tissue around the kidney so that retrospectively there is a greater amount of fat around the left than the right kidney, resulting from chronic perinephric infection.

Dr. Lerman: What about the expanded area in the kidney?

Dr. Hanelin: I do not have a good explanation for that. My personal thought was that the calyceal deformity probably resulted from an intrinsic renal lesion such as a carbuncle, but it may be that, with the amount of fibrous reaction about the kidney, extrinsic pressure alone could have produced the calyceal distortion.

Dr. Castleman: I think there was enough recent infection of the kidney to have helped produce this deformity.

CASE 41082

Presentation of Case

First admission. A seventy-year-old semiretired salesman was admitted to the hospital because of exertional dyspnea and fluid in the abdomen.

Ten years previously the patient noted crushing chest pain radiating down both arms, lasting five to ten minutes and relieved by rest and nitroglycerin. Eight years later he first noted shortness of breath on exertion and an awareness that "water was swishing around in the abdomen." He also noted protuberance of the abdomen, as well as leg edema that became worse during the day and subsided during the night. He was treated with digitalis and mercurial diuretics, with considerable relief of the edema. He had voluntarily discontinued digitalis because it made him nauseated. When leg edema, marked ascites, exertional dyspnea and orthopnea recurred he was admitted to the hospital.

He could not recall ever having been told of previous heart illness. He denied rheumatic fever or rheumatic equivalents. Five years before admission he had been hospitalized for gas pains thought to be caused by heart trouble. He had always been employed as a salesman, and stated that his alcoholic intake was "by no means slight" but that his diet had always been good. There was no history of jaundice, melena or clay-colored stools.

Physical examination revealed a well developed, well nourished man with slight cyanosis and moderate dyspnea. The neck veins were distended to the level of the mastoids at a 30° semireclining position. There was a moderate dorsal kyphosis, with increase in the anteroposterior diameter of the chest and a concavity of the lower sternum; the leaves of the diaphragm were high. There was diminished excursion of the lungs, and the breath sounds were vesicular. The lungs were resonant to percussion, and fremitus was diminished. The heart was enlarged, extending to the midaxillary line in the sixth intercostal space, and there was dullness to the right of the sternum. The pulmonic second sound was louder than the aortic. There was a Grade 2 blowing systolic murmur at the apex transmitted to the axilla, and a loud first mitral sound. One observer heard a brief mid-diastolic rumble at the apex. A blowing Grade 1 aortic systolic murmur, which was not transmitted, was heard. The abdomen was greatly distended, and the umbilicus everted. A visible venous pattern in the stretched abdominal skin was observed. There was a fluid wave and shifting dullness. No abdominal organs were palpable. The rectal sphincter was patulous; the prostate was smooth and enlarged to twice the normal size. There was pitting edema of the sacrum, penis, scrotum and legs.

The temperature was normal, the pulse 70, and the respirations 35. The blood pressure was 160 systolic, 60 diastolic.

The urine gave a + test for albumin and was otherwise normal. Examination of the blood revealed a hemoglobin of 12.4 gm. per 100 cc. and a white-cell count of 5300, with a normal differential. The sodium was 134 milliequiv., and the chloride 101 milliequiv. per liter; the nonprotein nitrogen was 42 mg., and the serum protein 6.8 gm. per 100 cc., with an albumin-globulin ratio of 1.3. Cephalin flocculation was negative, as was the blood Hinton test. A film of the chest showed diffuse enlargement of the heart, with bilateral prominence of the pulmonary vascular shadows (Fig. 1). A barium-swallow examination outlined a normal esophagus. An electrocardiogram demonstrated atrial fibrillation, with a slow ventricular rate, averaging 40, and rare ventricular premature beats. The T waves were inverted in Leads 1 and aVL, upright in Leads 2, 3, aVF and V_1 through V_3, and diphasic in Leads V_4 through V_6. Small R and deep S waves were present in Leads V_1 through V_5.

The patient improved rapidly on digitoxin, mercurial diuretics and salt restriction. He was discharged edema free on the tenth hospital day and advised to follow the outlined plan of digitoxin and salt restriction.

Second admission (eleven months later). He had been able to work part time as a salesman, which had necessitated being on the road much of the time, and he had occasionally been unable to restrict the salt intake. He had taken digitalis sporadically, omitting it on occasions because of nausea. He was readmitted to the hospital because of exertional dyspnea, peripheral edema and reaccumulation of ascites.

Physical findings were unchanged. The blood pressure was 188 systolic, 115 diastolic. The film of the chest was similar to the previous one, as were laboratory examinations. An electrocardiogram showed atrial fibrillation, with an irregular, slow ventricular rate and occasional premature ventricular beats, with minor ST-segment and T-wave changes of no diagnostic significance. He was treated with lanatoside C (Cedilanid), mercurial diuretics and salt restriction and discharged considerably improved on the twenty-sixth hospital day.

Third admission (one month later). In the interval he had required nitroglycerin twice for smothering feelings in the chest. He had extreme dyspnea on slight exertion, but denied paroxysmal nocturnal dyspnea or substernal pain. In the past month he had had one injection of meralluride sodium with theophylline (Mercuhydrin) and had taken Digoxin daily, but had noticed a 17-pound weight gain, most of which he thought had accumulated in the abdomen.

An abdominal paracentesis yielded 46 kg. of ascitic fluid. Examination of the fluid revealed 7900 red cells and 386 neutrophils per cubic millimeter and 4.2 gm. per 100 cc. of protein. The total serum protein was 5.7 gm., and the albumin-globulin ratio 1.2. The patient felt greatly improved after paracentesis and was discharged on the fourth hospital day after a total weight loss of 30 pounds.

Fourth through twelfth admissions (during the following eight months for relief of dyspnea and ascites). Physical examination revealed an enlarged heart extending to the anterior axillary line, with a Grade 3 blowing apical systolic murmur. The blood pressure varied from 200 systolic, 70 diastolic, to 140 systolic,

40 diastolic, but averaged about 170 systolic, 70 diastolic. There was massive ascites and marked leg edema. No abdominal organs or masses could be palpated. During this period the patient was maintained on a low-salt diet, Digoxin, ammonium chloride and frequent injections of mercurial diuretics. He had occasional tightness in the chest or smothering that was relieved by nitroglycerin. During each hospital admission, a paracentesis was done, with removal of 4 to 8 liters of cloudy, yellow fluid, after which he felt much more comfortable and, on discharge, returned to work until forced again to seek relief of dyspnea.

In the twelfth admission urinalysis showed a + + + + test for albumin and + test for bile; the sediment contained 3 red cells and many large hyaline casts per high-power field.

Final admission (approximately two years after the first admission). Since the last discharge the patient had been able to work. On the day of admission while at work he suddenly became very dyspneic and had severe pain in the anterior part of the chest.

On arrival at the hospital he was cyanotic, severely dyspneic and agitated. The neck veins were distended. There were moist rales two thirds of the way up each lung field. The heart sounds were largely obscured by the labored breathing. There was massive ascites, but no palpable organs or masses. The genitalia were edematous, and there was + + + pitting edema of the extremities to the midthighs. The skin of the lower legs was thickened, and there were scattered areas of ulceration.

The temperature was 102°F., the respirations 34, and the pulse 78 and regular. The blood pressure was 220 systolic, 80 diastolic.

The hemoglobin was 13.8 gm. per 100 cc., and the white-cell count 21,300, with 88 per cent neutrophils.

The patient was given meralluride sodium with theophylline, aminophylline and morphine intravenously and oxygen by mask. Tourniquets were applied. There was some improvement during the first four hours, but he became progressively less responsive. The neck veins became greatly distended, and rales were heard at the apexes. The pulse became feeble, and the blood pressure unobtainable. He died eight hours after admission.

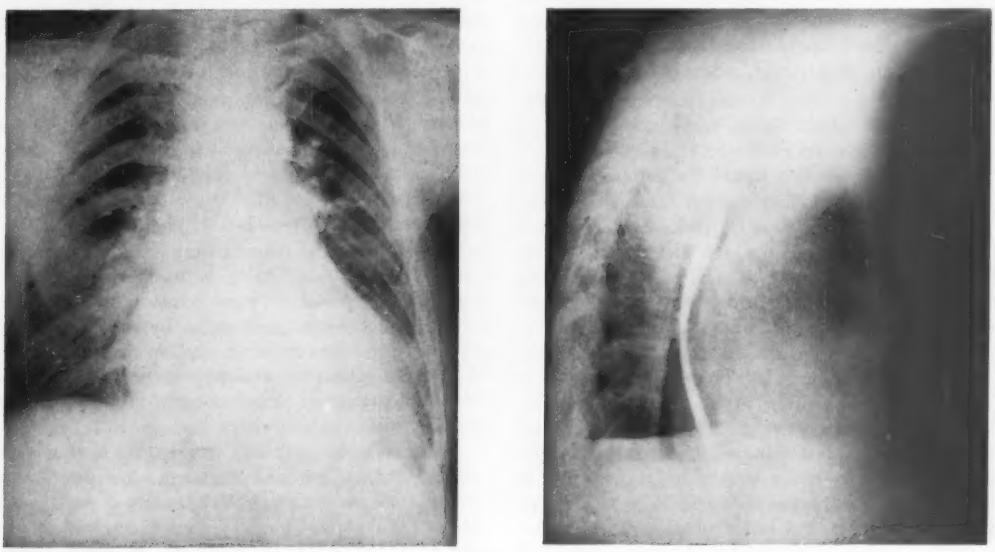

FIGURE 1. *Posteroanterior and Lateral Views of the Chest, Showing the Greatly Enlarged Heart and Congested Pulmonary Vessels.*

DIFFERENTIAL DIAGNOSIS

DR. JAMES H. CURRENS*: This seventy-year-old man gave a history of chest discomfort, quite characteristic of angina pectoris occurring on effort and relieved by rest, for a period of twelve years. He had a final four-year-period of chronic congestive heart failure with anasarca and a great deal more ascites than one usually sees in patients with chronic congestive heart failure, which perhaps suggests total failure of the heart. May I see the x-ray films before I proceed with the discussion of the differential diagnosis?

DR. JOSEPH HANELIN: Films made during the first and second admissions show the same findings. The heart is tremendously enlarged, probably with some preponderance of the left ventricle, if one has to pick out a particular chamber (Fig. 1). The left atrium is probably not a large chamber, but may be somewhat larger than normal — at least the esophagus is pushed more posteriorly than usual. This displacement could also result from massive enlargement of

*Assistant in medicine, Massachusetts General Hospital.

the heart. The pulmonary vessels are engorged, particularly in the lung roots, and are well seen on the right side, where they are not covered by the heart; there is also some congestion peripherally, but not as marked. There is probably just a minute amount of fluid in each costophrenic sulcus.

DR. CURRENS: Certainly a heart that has a point of maximum impulse in the sixth intercostal space at the midaxillary line is greatly enlarged, and certainly it appears enlarged in the x-ray film, without any characteristic configuration. I should expect that the whole heart was enlarged and that any pressure on the esophagus was due to the total enlargement and dilatation, predominantly dilatation, of the heart.

I had an opportunity to review the 5 or 6 sets of electrocardiograms taken during the various admissions. One taken about eleven years before death revealed a regular ventricular rate at 100, but I could see no P waves. Whether atrial fibrillation was present at this time or whether the PR interval was prolonged and the P waves superimposed on the T waves, I think, is impossible to say. In view of the subsequent persistent atrial fibrillation, I suspect that atrial fibrillation and perhaps a nodal rhythm account for the regular rate in the first tracing. Subsequent electrocardiograms gave evidence of atrial fibrillation. The striking feature was the slowness of the ventricular rate, which was often as low as 40, sometimes regular and sometimes irregular; the T-wave "pattern," if there is such a thing, was certainly not characteristic of any particular type of heart disease. The findings were consistent with an enlarged heart, enlarged left ventricle, but not characteristic of hypertensive heart disease, with which there are large R waves in the precordial leads on the left.

The problem is to decide the etiology of the heart disease. We can speak of a few only to discard them. Congenital heart disease is quite unlikely in a man of this age. The most probable congenital defect to account for some of the findings is a moderate defect of the interatrial septum that would result in atrial fibrillation, an enlarged heart and a prolonged course. The x-ray film certainly did not suggest the dilated pulmonary arteries that are usually present in conjunction with the atrial defect, and the electrocardiograms did not give evidence of hypertrophy of the right ventricle.

Did the patient have rheumatic heart disease? There was no history of joint pains or rheumatic fever. Elderly men with large emphysematous chests may have aortic regurgitation, without its being detected by auscultation. If a murmur is heard, it may be heard only at the apex. The large pulse pressure may be in favor of that diagnosis, but I am inclined to discard such a diagnosis because a diastolic murmur should be heard in a patient with aortic regurgitation sufficient to produce this degree of cardiac enlargement. Active rheumatic myocarditis is occasionally found in elderly patients who die in congestive heart failure, but that seems unlikely in this man, who had such a prolonged course. I should mention the group of patients who have atypical mitral stenosis. "Atypical" refers chiefly to the fact that the auscultatory findings are atypical; the remainder of the findings are usually typical of a high degree of mitral stenosis, in which the murmur is either poorly heard or not heard at all and in some cases has been heard in the past and has disappeared. This is an increasingly important group because the patients can frequently be helped by surgery. About 15 such patients have been observed in this hospital in the last three or four years.[1] An apical rumbling diastolic murmur was heard in the patient under discussion, but it was heard only once. Moreover, enlargement of the heart to this degree, with dilatation of the left ventricle, can result in a relative mitral stenosis, with the production of a murmur. A systolic murmur is probably a result of dilatation of the left ventricle and some degree of mitral regurgitation. I think it is unlikely that rheumatic heart disease was the cause of the trouble.

Hypertensive heart disease has to be considered but not very seriously. The hypertension was predominantly systolic, with only one diastolic reading above the range of normal. Systolic hypertension usually does not produce cardiac hypertrophy or dilatation of this degree. It was somewhat paroxysmal, and I think the chance that pheochromocytoma caused this picture is very remote.

Coronary-artery disease has to be seriously considered, for it is by all odds the most likely diagnosis in a patient of this age. There are a few atypical features for coronary-artery disease, however. There was no prolonged bout suggesting myocardial infarction, which would be unusual although it would not completely exclude coronary-artery disease in a patient with enlargement of the heart of this degree. Moreover, this patient's electrocardiograms would be quite unusual in a patient with coronary-artery disease with extensive scarring. There were no striking Q waves in the electrocardiogram, and the R waves across the precordium were of good amplitude.

Thyrotoxic heart disease might be considered but only in passing. The wide pulse pressure and atrial fibrillation are consistent with that diagnosis, but the ventricular rate was slow — one would expect a faster rate with thyrotoxicosis.

Amyloidosis of the heart is a rare condition. There was no mention of enlargement of the tongue, which is associated with primary amyloidosis, and it is primary amyloidosis that usually affects the heart.

Pericardial effusion or constrictive pericarditis is unlikely to produce a course of this nature. Constrictive pericarditis is usually associated with a heart of normal size or only slightly enlarged. Pericardial effusion may cause enlargement of this degree but would not result in the protracted course that this patient had.

What am I left with? There is a condition, which

I strongly suspect that this patient had, that is being recognized more frequently and has been discussed in these conferences on two occasions in the last eighteen months,[2,3] known as idiopathic hypertrophy of the heart with endocardial fibroelastosis. That is an elaborate name, but it is purely descriptive. The unusual feature in the 2 patients previously discussed was the presence of angina pectoris for varying periods. One of these described recently by Drs. White and Fennell,[4] had angina pectoris, mild perhaps, over a period of fifteen years. The patient under discussion gave a history of angina pectoris over a period of twelve years. A few features about this illness are worth emphasizing. One is that the heart usually is greatly dilated. There is usually a picture of total heart failure similar to that which this patient demonstrated in that all the chambers of the heart are dilated, with resulting extensive anasarca. For that reason patients have occasionally been subjected to exploration for the relief of constrictive pericarditis, which was not found. However, the patients who were operated on had hearts that were not nearly this large, and they were younger. Most of the patients with idiopathic hypertrophy have atrial fibrillation, as in the 2 cases previously discussed, which I think results from enlargement of the heart rather than from any specific characteristic of the heart disease. Peripheral emboli originating from a mural thrombus in the left ventricle are common. There was no good evidence of peripheral embolization in the case under discussion unless renal infarction produced the slight degree of hematuria on one of the two admissions. The kidneys, however, are a likely site for embolization from the left ventricle. I suspect that the condition is more common in males — at least the adult patients who have been seen in this hospital have been predominantly males.[5]

The amount of ascites that this patient had is disturbing and raises the possibility of congestive cirrhosis of the liver. I should suspect some degree of fibrosis characteristic of congestive cirrhosis. The protein in the ascitic fluid is unusually high for a pure transudate and, in a patient of this age, raises the question of a complicating tumor, perhaps a hepatoma or a metastatic carcinoma of the liver.

The cause of death seems to have been acute failure of the left ventricle, with the rapid accumulation of fluid in the lungs, rather than pulmonary embolism although that is also a possibility; certainly, the rapid onset of the dyspnea and chest discomfort were in keeping with that diagnosis. I therefore suspect that the patient had idiopathic hypertrophy, with fibroelastosis. This diagnosis is made on the assumption that lightning can strike in the same place thrice in eighteen months.

DR. ROBERT S. PALMER: I blush to confess that I did not think of Dr. Currens's persuasively presented diagnosis, and I hope for his sake and my instruction that it is correct. As I heard the story I thought I had either seen this patient or seen others like him. I wondered whether this was the "death-of-a-salesman" situation, which was hinted by his admission that the alcoholic intake had been considerable. I think he had coronary-artery disease with angina pectoris and probably some thromboses and infarctions. I do not think there was enough evidence for the diagnosis of rheumatic heart disease. Nor was there clear-cut, definite evidence — complete with obvious murmurs and a large pulsating liver — on which to base the diagnosis of cardiac cirrhosis. Therefore, I thought he had coronary-artery disease and alcoholic cirrhosis. Did he have spider angiomas or anything else indicative of liver failure?

DR. H. ROTHBERG: He had no spider angiomas and no liver palms; the liver had not been felt because of the ascites. On the last two admissions he did have a fetor hepatis.

DR. PALMER: I should suppose that, after the ascitic fluid had been removed, a large liver would have been felt if he had only congestive heart failure to account for the ascites.

DR. BENJAMIN CASTLEMAN: What caused the large heart? Do you think hypertension was a factor?

DR. PALMER: I suppose that there may have been some hypertensive heart disease.

A PHYSICIAN: Could this have been beriberi heart disease?

DR. PALMER: The patient was said to have kept up his food intake, but I suppose that it could have been.

DR. CURRENS: The ventricular rate is usually quite rapid in beriberi heart disease, and the rate in the case under discussion was slow.

DR. CASTLEMAN: Dr. Rothberg, do you have any comment?

DR. ROTHBERG: No; except that the systolic murmur was quite loud, Grade 3 to Grade 4, and also that it disappeared during the terminal illness.

CLINICAL DIAGNOSES

Congestive heart failure.
Coronary-artery disease.
Cardiac cirrhosis of liver.

DR. JAMES H. CURRENS'S DIAGNOSES

Idiopathic cardiac hypertrophy, with fibroelastosis.
Congestive heart failure.

ANATOMICAL DIAGNOSES

Coronary-artery disease, severe.
Cardiac hypertrophy and dilatation, hypertensive type.
Anasarca, with marked ascites.
Chronic passive congestion of liver.
Pulmonary emphysema.
Bronchopneumonia.

Pathological Discussion

Dr. Castleman: At autopsy, as one might have surmised, there was a great deal of fluid. We found 10 liters of fluid in the abdomen, about 1 liter in each side of the chest and excessive fluid even in the pericardium. The heart was tremendous in size, weighing 700 gm., and was diffusely hypertrophied, through all chambers, and with a fair amount of dilatation. There were no valvular lesions and no endocardial fibroelastosis; at least there was no thickening of the endocardium that we could find on gross examination, and that was borne out by microscopical examination. The only type of heart disease that we could find structurally besides the hypertrophy was the severe coronary-artery disease, arteriosclerosis with pinpoint lumens and in some places occlusion of the vessels.

Microscopical examination showed foci of a fairly extensive diffuse myocardial fibrosis — healed infarction. We looked carefully around the orifice of the inferior vena cava, hoping to find narrowing, because I did not recall any case of chronic congestive heart failure with as much ascites as this patient had over such a short period, but we were unable to find any. The liver, Dr. Palmer, was perfectly normal in size and weighed in fact less than normal; it was not scarred, and microscopically we found no evidence of fibrosis. There was only central congestion. I am afraid I shall have to end up by saying that this patient had the usual variety of hypertensive heart and coronary-artery disease, which for some unknown reason produced an extreme amount of ascites.

Dr. Palmer: This marked ascites without liver enlargement in congestive heart failure is certainly unique in my experience. I am chastened.

Dr. Castleman: Terminally, the patient had some bronchopneumonia; he did not have much emphysema. The kidneys were slightly scarred, but not enough to produce renal failure.

Dr. Reed Harwood: I am wondering if an important feature of this case was that he had not been taking good care of himself between the hospital admissions — that he ate a great deal of salt and continued drinking.

Dr. Castleman: He was in the hospital so much in the last two years that his diet could not have been neglected.

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Bookplate Collection of the Boston Medical Library

2. The Hyams collection was founded by a gift of $25,000, with the result that a valuable library of manuscripts and books has been built up, dating from about 1200 A.D. to the present time. The bookplate is symbolic. The motto, loosely translated, reads, "To be enlightened by the light of life." The central figure holding an open book, with an astronomic instrument on the side, is that of a medieval physician, probably Maimonides. On the left is the single staff with serpent, and on the right the Menorah, or seven-branched candelabra. Below the portrait is the six-pointed star enclosing the word "truth" and surmounted by a crown. The star is supported by two lions, and below are two shofars, the ritual horn of Israel. The columns list the names of famous books and persons: on the left, Isaac Israeli (Judaeus), Avicenna, Maimonides, Naton Ha Meati, Jacob Zahlon, Tobias and Solomon ibn Ya'ish; and on the right, the Bible, the Talmud, Galen, Hippocrates, Boda of Asaph, Alrazi and Donolo. Artist: David Rose.

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FELLOWSHIP: A PRIVILEGE AND A RESPONSIBILITY

REGULARLY each year statements for fellowship dues in the American Medical Association are distributed via the offices of the Massachusetts Medical Society, and regularly each year those for the Massachusetts Medical Society assessment are deployed in similar fashion. In addition a number, although not all, of the district societies make their own demands on their membership through their local treasurers.

The system — or the three systems — is not hopelessly complicated, but such is the tendency of human kind to procrastinate, fail to read or to give attention, disregard, forget, overlook, bypass and throw into the wastebasket, that a repetition of the responsibilities involved and the penalties attached to repeated failures to comply with the fiscal requirements of membership in these bodies may be in order.

Fellowship in the Massachusetts Medical Society is contingent on membership in a district society, in addition to which all fellows, with certain exceptions, are required to pay annual assessments and are entitled to receive the *Journal*. The exceptions are as follows: honorary and associate fellows are not required to pay dues but are entitled only to those rights and privileges of the Society that permit them to attend and address meetings. Nonresident fellows pay a reduced assessment, receive the official publications of the Society and may attend meetings but have no other privileges.

Fellows, on the other hand, who have reached the age of sixty-five years and are in good standing in the Society may, on application to the Secretary or the Treasurer, become senior fellows. As such they retain all the rights and privileges of active fellowship but without the payment of dues. They may receive the *Journal* without payment, on *annual* application to the editorial offices. Retirement from practice before age sixty-five does not of itself constitute eligibility for senior fellowship.

Other fellows may have their dues reduced or remitted by the Executive Committee if sufficient cause is shown to the Committee on Membership, in whose hands such recommendations lie. Hospital residents may fall in this class if financial hardship is invoked, as may older fellows who cannot keep up with their commitments because of ill health or other physical handicap. The intercession of a medical-school dean or hospital administrator on behalf of a faculty member or research fellow who pleads financial hardship is honored by the Committee. Each of these exceptions, however, constitutes a separate case to be decided on its own merits; no groups, such as hospital residents, are automatically exempted from paying dues.

And woe betide the fellow who for two consecutive years has defaulted either his Massachusetts Medical Society or his district dues; for the gate is wide and the way is broad that leadeth to destruction, and hav-

ing disregarded his semiannual notices and the final warning by registered mail, he has no recourse when the Executive Committee, acting on the report of the Committee on Membership, automatically, as required by the *By-laws*, deprives him of the privileges of fellowship. The mere payment of arrears is not then enough for his return into the Society. He is out, and step by step he must re-enter the ranks, first on recommendation of his district-society committee on membership, then on recommendation of the Committee on Membership of the state society, and finally on vote of the Executive Committee. Then and then only is he permitted to discharge his indebtedness and start anew the enjoyment of such intangible privileges as the hospital staff membership that may have been lost with the deprivation of fellowship.

Less serious to some fellows, especially the nonreaders, although prompter in operation, is the discontinuance of *Journal* subscriptions that takes place in early spring for those fellows who have not paid their dues of the immediately preceding January. Each year some thousand names are thus removed from the mailing list, a great company compared to the 40 or 50 who are deprived of membership for nonpayment. The simple payment of indebtedness restores their stencils to the active file, but the lost issues are lost indeed, for the number of journals printed has been reduced to the number required by the active list.

A little time before the distribution of the Massachusetts Medical Society bills, the American Medical Association statements are extruded from Society headquarters early in the winter. These bills for $25 cover fellowship in that august organization and subscriptions to the *Journal of the American Medical Association*. Whereas fellowship in the Association is contingent on fellowship in the state society — and payment of the A. M. A. dues — the reverse is not true in this state. Loss of membership in the American Medical Association for non-payment of dues does not affect state membership, although it may affect the state society's representation in the House of Delegates.

The age at which a fellow becomes eligible for retired fellowship in the national association is seventy, regardless of the fact that he may already have achieved senior fellowship in the Massachusetts Medical Society. However, if the dues of a fellow who has not yet qualified for senior fellowship are remitted by the Society for good reasons, and proper presentments are made to the American Medical Association, the latter will commonly co-operate and do likewise.

INFLUENZA IN 1955

In a recent editorial in the *Journal of the American Medical Association* Dr. Dorland J. Davis,[1] of the National Microbiological Institute, briefly reviewed the occurrences of influenza epidemics in this country and elsewhere in recent years, in relation to the types of influenza virus that caused them. Influenza C virus, the most recent type to be recognized,[2] is associated with mild sporadic illnesses. Influenza B virus has caused many localized outbreaks that reached epidemic proportions in the winters of 1940, 1945 - 46 and 1952.

Influenza A virus has been the cause of most of the widespread epidemics, and these have occurred in the United States every two or three years, the last ones being in the winters of 1951 and 1953. There has been a progressive change in the antigenic compositions of strains of influenza A viruses causing outbreaks, although the strains recovered in any one year have been remarkably uniform in this respect. During the epidemic of 1947 a major change in the antigenic composition of the influenza A viruses was recognized; all strains that have been isolated during that year and since then have differed markedly from those of previous years. To this change was ascribed the failure of the influenza vaccines used during that season to protect against the influenza when it occurred, since the vaccine contained only strains isolated in previous years.[3] Influenza A infections were not recognized in the United States or in Western Europe during the winter of 1953 - 54, although there was very close surveillance throughout the season by many workers interested in the World Health Organization Influenza Study Program.

On the basis of the pattern of the periodic recurrences of influenza A and B, the pattern of the mortality rates for influenza and pneumonia in recent years and the types of influenza viruses that have caused the most recent epidemics in this and other countries, Dr. Davis predicts that influenza A outbreaks may occur in some sections of the United States during this winter or the following one. This prediction is also based, in part, on the fact that outbreaks of influenza A infection were identified in Australia in May and June, 1954, in Johannesburg, South Africa, in June and July, and in the Philippines in August, when there was also a recurrence of influenza in Australia.[4]

Since the 1953 epidemic, influenza A had not been recognized in this country as of the middle of January, 1955 — at least none had been reported in the Weekly Epidemiological Record of the World Health Organization or in the Weekly Communicable Disease Summary issued by the National Office of Vital Statistics. However, in the latter summary for the week ending January 29, there are reports of identification of influenza viral infections from widely scattered areas. These include reports of 3 cases from Washington, D. C. (identified at the National Microbiological Institute), 1 from the Minnesota Department of Health and some from a localized outbreak in Western Canada in the vicinity of Calgary, Alberta. The illnesses in Washington began during the third week in January; the patient in Minnesota was ill during the middle of January, and the cases in Alberta began early in January. Influenza B was identified in all these

areas, either by isolation and characterization of the virus or by rises in antibody titers specific for Type B influenza in the patients' serum. Outbreaks have also been reported in widely scattered areas in the United States, but the specific strain of virus has not been identified in those areas. The last report of the occurrence of influenza B in this country was of a localized outbreak at the Great Lakes Naval Training Station in Illinois.[5]

If these occurrences are any portent of what is in the offing, they may be taken as evidence that an epidemic of influenza B may be imminent, or is actually in progress in many parts of this country. The multiple simultaneous foci suggest that this epidemic may be even more widespread than the one that occurred in 1952. The influenza B epidemic that was observed in 1945 - 46 was accompanied by a particularly high morbidity rate in some localities near Boston,[6] but in that year prophylactic vaccination, using vaccines that incorporated influenza B virus, was found to be successful by many observers.[3] There have been years when both influenza A and B viruses were encountered either simultaneously or in succession, but usually only one of these types has predominated. It will be interesting to observe whether, during the remainder of the winter, primarily influenza A infections, as Dr. Davis had anticipated, an influenza B epidemic, as these findings suggest, or outbreaks of both types of infection will be encountered.

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FRANK H. LAHEY MEMORIAL AWARD

THE presentation of the Frank H. Lahey Memorial Award to President Eisenhower on November 16 represents an event of threefold significance.

The award was established by the National Fund for Medical Education with the joint participation of the American Medical Association and the Association of American Medical Colleges. The Fund, initiated in 1949, has in this way marked the conclusion of the first five years of a successful program to aid medical education. During this time it has obtained the interest and financial support of the lay public in co-operating with the medical profession and has contributed almost $7,000,000 in grants to the 80 medical schools of the United States.

The first award was given to President Eisenhower in recognition of his help in founding the National Fund for Medical Education in 1949, when he was President of Columbia University, and of his continued support since that time. Along with former President Herbert Hoover, Dr. James B. Conant, then president of Harvard University, and other educators,

as well as leaders in business and various professions, he helped to work out plans "to keep medical education free, solvent and progressive." These plans have operated effectively to mobilize private support for the medical schools. The needs that have thus been met in part will require continuing attention, and it is the intention of the three participating organizations to give periodic recognition in the future to other laymen who show outstanding leadership in the cause of medical education.

The award bearing the name of Dr. Frank H. Lahey will serve as a permanent memorial to the man who

has been given highest credit for bringing the problems of the nation's medical schools before the professional and lay public. Dr. Lahey was one of the Fund's founding trustees and was active in its leadership during the later years of his life. He became known as one of its most effective spokesmen.

Physicians who have heard Dr. Lahey speak at medical meetings and who have read his medical publications recall his unique ability as a teacher of physi-

cians and his strong influence in professional affairs. It is noteworthy that in his efforts to promote support of medical schools, he made a similar impression on business executives and civic leaders. One listener is said to have remarked, "When that fellow gets through talking you not only *know* the problem, you *feel* it."

Friends and colleagues of Dr. Lahey will feel gratified with the establishment of the Frank H. Lahey Memorial Award and with the selection of the first recipient as an indication of the high level of achievement with which this award will be associated in the future.

EDINBURGH MEDICAL JOURNAL

1805-1954

THE news that the *Edinburgh Medical Journal* suspended publication after its issue of December, 1954, comes as a shock to those who have respected and admired this literary product of one of the older and certainly one of the most eminent centers of medical culture. The journal's final appearance came on the completion of its hundred and fiftieth year of uninterrupted publication.

Tracing its origin, according to the *British Medical Journal,* to *Medical Essays and Observations,* published from 1733 to 1744, the distinguished Scottish publication made its initial appearance in January, 1805 as the *Edinburgh Medical and Surgical Journal.* In continuous publication since that time it has finally succumbed to rising costs and diminishing revenue.

Published under its original name for fifty years, the journal then shortened its title to that by which it has been known for the past century. Since 1861 it has been published and printed by the firm of Oliver and Boyd in Tweeddale Court, off High Street, Edinburgh. Another relic of Caledonian tenacity, this firm was established in 1778 in the same stone buildings that today house its offices and press.

The *Edinburgh Medical Journal* may be presumed to have been, at the time of its cease fire, the oldest medical periodical in continuous existence — certainly in the English language. With its discontinuance it becomes probable that this mantle has fallen on the *New England Journal of Medicine,* established in January, 1812, as the *New England Journal of Medicine and Surgery,* continuing as the *Boston Medical and Surgical Journal* from 1828 until 1928, when it assumed its present name.

The *Boston Medical and Surgical Journal* was formerly owned — as was the *Edinburgh Medical Journal* — by a group of physicians, and itself came near to extinction after World War I despite a distinguished editorship, which the Edinburgh journal has also enjoyed. Its purchase by the Massachusetts Medical Society in 1921 rescued this journal, and its subsequent course has demonstrated the advantages of a strong yet liberal sponsorship.

Industrial Pathology. — . . . . *The chief disease amongst tailors is fistula; amongst bakers, scrofula and skin diseases; the latter are advised to rub their hands with oil, to prevent the flour insect and weevils from irritating the skin. . . . The most dangerous part of the painter's trade is "flatting," white lead, turpentine, and closely-heated rooms, generating colic: the remedy is sulphuric acid,* cleanliness, *tubs of water and fresh air; and, as an antidote, the more frequent use of "white zinc" or "zinc lead."*

Boston M. & S. J., *March 1, 1855*

MASSACHUSETTS MEDICAL SOCIETY

TREASURER'S OFFICE

This year the Committee on Finance has voted a refund of $6000 to the district societies from the surplus in the General Fund at the end of 1954.

Members are reminded that the percentage of this sum that is allocated to their own district is determined by the number of dues from that district paid by March 1, 1955. Members who have not paid their dues by this date are automatically removed from the mailing list of the *Journal* until such dues are paid.

ELIOT HUBBARD, JR.
Treasurer

DEATHS

BUTTERS — Charles M. Butters, M.D., of Somerville, died on February 1. He was in his fifty-fourth year.

Dr. Butters received his degree from Tufts College Medical School in 1937. He was a member of the staffs of the Somerville, Booth Memorial and Cambridge Tuberculosis hospitals and a fellow of the American Medical Association.

He is survived by his widow, two brothers and two sisters.

CURTIN — William E. Curtin, M.D., of Plymouth, died on February 3. He was in his sixty-seventh year.

Dr. Curtin received his degree from Baltimore Medical College in 1913. He was physician for the county house of correction, a member of the Massachusetts Society of Examining Physicians and Massachusetts Medico-Legal Society, a fellow of the American Medical Association and, formerly, medical examiner for the Third Plymouth District and president, Jordan Hospital and Plymouth County Health Association.

He is survived by his widow, two daughters, a sister and a brother.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS

ORTHOPEDIC CLINIC	DATE		CLINIC CONSULTANT
Gardner	March	1	Carter R. Rowe, M.D.
Haverhill	March	2	William T. Green, M.D.
Greenfield	March	3	Charles L. Sturdevant, M.D.
Lowell	March	4	Albert H. Brewster, M.D.
Salem	March	7	Paul W. Hugenberger, M.D.
Brockton	March	10	George W. Van Gorder, M.D.

Lynn*	March 14	Daniel M. Killoran, M.D., and John J. Crowley, M.D.
Springfield	March 15	James D. Fisher, M.D.
Pittsfield	March 16	Edward J. Coughlin, Jr., M.D.
Hyannis	March 24	Paul L. Norton, M.D.
Worcester	March 25	John W. O'Meara, M.D.
Fall River	March 28	David S. Grice, M.D.

Rheumatic-Fever Clinic	Dates
Fitchburg	March 1, 8, 15, 22, 29
North Reading	March 2, 9, 16, 23, 30

Plastic Clinic	Held	Consultant
Eastern Massachusetts	Semi-monthly	Bradford Cannon, M.D.
Western Massachusetts	Monthly	Joseph M. Baker, M.D.

Physicians referring new patients to clinic should get in touch with the district health officer to make appointments. Patients are seen by appointment only.

*This clinic serves Lynn, Lynnfield, Saugus, Nahant, Revere, Chelsea, Everett and Winthrop. Referrals should be made directly to the Lynn Clinic.

NONCLINICAL NOTES

NATIONAL MUSCULAR DYSTROPHY RESEARCH FOUNDATION

The National Muscular Dystrophy Research Foundation and its research advisory board, of which Dr. Derek Denny-Brown, James Jackson Putnam Professor of Neurology, Harvard Medical School, is chairman, have announced the grant of $7000 for the first year of a three-year research project to Baylor College of Medicine, Houston, Texas.

Mrs. Dwight D. Eisenhower is national honorary president of the Foundation, and Ed Sullivan, Senator Price Daniel, Governor Allan Shivers and Mr. and Mrs. Roy Rogers are among the national sponsors. The Foundation was organized by two sisters, Sallie and Nadine Woods, victims of the disease.

NOTICES

NEW ENGLAND CARDIOVASCULAR SOCIETY

A meeting of the New England Cardiovascular Society will be presented by the New England Center Hospital and the Children's Medical Center in Morse Auditorium, Museum of Science, Boston, March 7 at 8 p.m.

The program is as follows:

New England Center Hospital. Dr. Samuel Proger, presiding.

Preliminary Studies in Man on the Antiarrhythmic and Pharmacologic Action of Ambonestyl (2-diethylaminoethyl-isonicotinamide). Drs. Byron B. Clark and Benjamin Etsten.

Pump Action and Reservoir Pressure. Dr. James W. Dow.

The Exchange of Cholesterol in the Gastrointestinal Tract in Normal Subjects and in Those with Various Abnormalities of Cholesterol Metabolism. Drs. Malcolm M. Stanley and Samuel Cheng.

Children's Medical Center. Dr. Benedict F. Massell, presiding.

The Application of the Antistreptolysin-O Test in the Evaluation of Joint Pain and in the Diagnosis of Rheumatic Fever. Drs. Sujoy B. Roy, George P. Sturgis and Benedict F. Massell.

Coarctation of the Aorta with Congestive Failure in Infants. Drs. Henry T. Lang, Jr., and Alexander S. Nadas.

Interatrial Gradients Compared with Relative Ventricular Work — a Possible Application of Starling's Law in Man. Drs. Walter T. Goodale, Roger B. Hickler, Leonard S. Sommer and Andreas Haemmerli.

Physicians and medical students are invited.

CHELSEA SOLDIERS' HOME

A professional-staff meeting will be held at the Chelsea Soldiers' Home in Quigley Memorial Auditorium on April 13 at 7:15 p.m. Dr. Samuel Levine will speak on the topic "Management of Cardiac Disease." All physicians are invited.

HARVARD MEDICAL SOCIETY

The Harvard Medical Society will present a symposium on the interrelation between pulmonary mechanics and gas exchange, arranged by the departments of Physiology, Harvard School of Public Health and Harvard Medical School, with J. L. Whittenberger presiding, in the auditorium, Jimmy Fund Building, 35 Binney Street, Boston, March 8 at 8 p.m.

The program is as follows:

Components of the Respiratory Dead Space and Their Variation with Pressure Breathing and with Bronchoactive Drugs. J. R. Pappenheimer and B. Folkow.

Some Mechanical Factors in the Distribution of Pulmonary Ventilation. J. Mead, M. D. McIlroy, N. J. Selverstone and E. P. Radford, Jr.

Factors Governing Elastic Properties of Mammalian Lungs. E. P. Radford, Jr., J. Mead and N. Lefcoe.

The Interrelation between the Pulmonary Circulation and the Elastic Properties of the Lungs. R. Frank, E. P. Radford, Jr., and M. McLaughlin.

AMERICAN GOITER ASSOCIATION

A meeting of the American Goiter Association will be held at the Skirvin Hotel, Oklahoma City, April 28 through 30. The topic of the meeting will be the physiology and diseases of the thyroid gland.

POSTGRADUATE COURSE IN OBSTETRICS AND PEDIATRICS

The Boston Lying-in Hospital and the Children's Medical Center, in co-operation with the Massachusetts Department of Public Health, will offer a postgraduate course in obstetrics and pediatrics for physicians April 7-9. The program will include lectures, conferences, clinical demonstrations, ward rounds and clinicopathological conferences. Applications may be made through Dr. Crawford Hinman, 1180 Beacon Street, Brookline.

NATIONAL VITAMIN FOUNDATION SYMPOSIUM

A symposium on the antimetabolites, their modes of action and therapeutic implications will be presented in conjunction with the tenth annual meeting of the National Vitamin Foundation at the Biltmore, New York City, on March 1, starting at 9 a.m. Further information may be obtained from the National Vitamin Foundation, 15 East 58th Street, New York 22, New York.

SOCIETY MEETINGS AND CONFERENCES

February–April. Postgraduate Medical Institute. Page 451, issue of September 9.

February–May. Sanitary Engineering Center Training Programs. Page 122, issue of July 15.

February 24 and 25. Pan-American Academy of General Practice. Page 496, issue of September 16.

February 25, March 11 and 25. Postgraduate Course in Occupational Medicine. Page 922, issue of November 25.

February 25. Phi Lambda Kappa Fraternity. Hyman Morrison Lecture. Page 289, issue of February 17.

February 25 and April 1. American Psychiatric Association (Massachusetts District Branch). Page 289, issue of February 17.

February 26 and 27. Mid-Winter Radiologic Conference. Page 1076, issue of December 23.

February 28. Consultation Clinics for Crippled Children in Massachusetts. Page 155, issue of February 17.

February 28–March 1. International College of Surgeons. Southwestern Division Regional Meeting. Page 157, issue of January 27.

February 28–March 2. American Orthopsychiatric Association. Page 994, issue of December 9.

February 28–May 9. Seminar in Psychiatry and Neurosurgery. Page 452, issue of September 9.

March 1. National Vitamin Foundation Symposium. Notice above.

March 1–30. Consultation Clinics for Crippled Children in Massachusetts. Page 328.

March 2. Pharmacology Seminar. Page 246, issue of February 10.

March 5. Massachusetts Academy of General Practice. Spring Clinical Assembly, Worcester.

MARCH 5–MAY 7. Middlesex South District Medical Society. Postgraduate Course. Page 758, issue of October 28.
MARCH 7–12. Course in Care of Atomic Casualties. Page 285, issue of August 12.
MARCH 7. New England Cardiovascular Society. Page 329.
MARCH 7–APRIL 18. Hartford Medical Society. Page 289, issue of February 17.
MARCH 8. Harvard Medical Society. Page 329.
MARCH 23–26. International Academy of Proctology. Page 876, issue of November 18.
APRIL 1. New England Society of Anesthesiologists. Page 289, issue of February 17.
APRIL 5. Microcirculatory Conference. Page 289, issue of February 17.
APRIL 7–9. Postgraduate Course in Obstetrics and Pediatrics. Page 329.
APRIL 8. Massachusetts Society for Research in Psychiatry. Page 679, issue of October 14.
APRIL 13. Chelsea Soldiers' Home. Page 329.
APRIL 13. New England Surgical Society. Spring Meeting. Boston.
APRIL 21 and 22. New York Academy of Medicine (Eastern States Health-Education Conference). Page 922, issue of November 25.
APRIL 28–30. American Goiter Association. Page 329.
APRIL 30. State University College of Medicine at New York City. Page 289, issue of February 17.
MAY 4 and 5. American Psychosomatic Society. Page 286, issue of August 12.
MAY 17–19. Massachusetts Medical Society. Annual Meeting. Hotel Statler, Boston.
JUNE 5 and 6. American Board of Physical Medicine and Rehabilitation. Page 794, issue of November 4.
JUNE 21–25. National Association for the Prevention of Tuberculosis. Page 540, issue of March 25.
AUGUST 28–SEPTEMBER 2. American Congress of Physical Medicine and Rehabilitation. Page 157, issue of January 27.
NOVEMBER 6–13. Second International Congress of Allergology. Page 157, issue of January 27.
NOVEMBER 29–DECEMBER 2. Interim Session of the American Medical Association. Boston.

CALENDAR FOR THE WEEK BEGINNING THURSDAY, MARCH 3

THURSDAY, MARCH 3
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:45–9:45 a.m. Cardiac Grand Rounds. Jimmy Fund Building, Children's Medical Center, 35 Binney Street.
*9:00–10:00 a.m. Surgical Rounds. Sherman Auditorium, Beth Israel Hospital.
*9:00–10:00 a.m. Arthritis Grand Rounds. Robert Breck Brigham Hospital.
*10:00–11:00 a.m. Combined Medical-Surgical Rounds. Sherman Auditorium, Beth Israel Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–12:00 m. Thoracic Conference. Open Heart Surgery in a Hypothermic State. Drs. William F. Bernhard, Hugh E. Wilson and Dwight E. Harken. Main Amphitheater, Peter Bent Brigham Hospital.
*11:00 a.m.–12:00 m. Medical Staff Conference. Sherman Auditorium, Beth Israel Hospital.
*11:00 a.m.–12:30 p.m. Hand Clinic (Physical Medicine and Rehabilitation Service). Boston City Hospital.
*12:00 m.–1:00 p.m. Surgical Staff Conference. Sherman Auditorium, Beth Israel Hospital.
*12:00 m.–1:00 p.m. Physiological Aspects of Aortic Valvular Disease. Dr. Harry Goldberg. Stearns Auditorium, New England Center Hospital.
*12:15–1:15 p.m. Tumor Clinic. Dr. T. W. Botsford. Amphitheater, Peter Bent Brigham Hospital.
*4:00–5:00 p.m. Pediatric Seminar. Burnham Memorial Hospital for Children (Burnham 4), Massachusetts General Hospital.

FRIDAY, MARCH 4
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*9:30–11:30 a.m. Medical and Surgical Grand Rounds. Drs. George W. Thorn and Francis D. Moore. Main Amphitheater, Peter Bent Brigham Hospital.
*10:00 a.m. Tuberculosis Surgical Clinic. South End Health Unit, 57 East Concord Street.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–1:00 p.m. Medical Grand Rounds. Dr. Proger and Staff. Stearns Auditorium, New England Center Hospital.
*1:30 p.m. Fertility and Endocrine Clinic. Free Hospital for Women, Brookline.
*1:30 p.m. Tumor Clinic. Mount Auburn Hospital, Cambridge.
*4:00–5:00 p.m. Child Psychiatry. Burnham Memorial Hospital for Children (Burnham 4), Massachusetts General Hospital.
*4:00–10:00 p.m. Alcoholism Clinic. By appointment. Washingtonian Hospital, 41 Waltham Street.

SATURDAY, MARCH 5
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Anesthesia Conference. Dr. Etsten. Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.
*8:30–10:00 a.m. Orthopedic Staff Conference. Boston City Hospital.
*9:00–10:30 a.m. Surgical Grand Rounds. Dr. Child and Staff. Stearns Auditorium, New England Center Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
10:30 a.m.–12:00 m. Middlesex South District Medical Society. Postgraduate Course. Office Management of Diabetes. Drs. Alexander Marble and David Hurwitz. Margaret Jewett Hall, Mount Auburn Hospital, Cambridge.
*11:00 a.m.–12:00 m. Hematology Clinic. Dr. William Dameshek. Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.

MONDAY, MARCH 7
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Medical and Surgical Clinic on Diabetic Problems. New England Deaconess Hospital.
*8:30–9:30 a.m. Clinic by Entire Surgical Staff and Anesthesia Staff. New Cheever Amphitheater, Dowling Building, Boston City Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*12:00 m.–1:00 p.m. Pediatric Clinicopathological Conference. Drs. MacMahon and Baty. Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.
*12:00 m.–1:00 p.m. Metabolism Conference. Dr. Schwartz. Stearns Auditorium, New England Center Hospital.
*12:15–1:15 p.m. Clinicopathological Conference. Main Amphitheater, Peter Bent Brigham Hospital.
*1:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*4:00 p.m. Clinicopathological Conference. Pathology Conference Room, Beth Israel Hospital.
*4:00–5:00 p.m. Surgical Pathology. Dr. MacMahon. Stearns Auditorium, New England Center Hospital.
*4:00–5:30 p.m. Literature Conference. Dr. Burnap. Peter Bent Brigham Hospital.
*5:00–6:30 p.m. Anesthesia Group of the Lahey Clinic. Joslin Auditorium. New England Deaconess Hospital.
7:00–8:00 p.m. Pathology Conference. Dr. MacMahon and Staff. Stearns Auditorium, New England Center Hospital.
*7:00–9:00 p.m. Slide Seminar in Pathology. Dr. MacMahon. Stearns Auditorium, New England Center Hospital.
*8:00 p.m. New England Cardiovascular Society. Morse Auditorium, Museum of Science, Boston.
8:30 p.m. Hartford Medical Society. Routine Orders and Humbug. Dr. Samuel P. Harbison. Hunt Memorial Building, Hartford.

TUESDAY, MARCH 8
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*9:00 a.m. Geriatrics Clinic. Peter Bent Brigham Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*12:00 m. Pediatric Grand Rounds. New Cheever Amphitheater, Dowling Building, Boston City Hospital.
*12:00 m.–1:00 p.m. Pediatric Combined Rounds. Burnham Memorial Hospital for Children (Burnham 4), Massachusetts General Hospital.
*12:00 m.–1:00 p.m. Endocrine Conference. Dr. Astwood. Stearns Auditorium, New England Center Hospital.
*12:15–1:15 p.m. X-Ray Conference. Dr. Merrill Sosman. Main Amphitheater, Peter Bent Brigham Hospital.
12:30–1:30 p.m. Medical Journal Club. Joslin Clinic. New England Deaconess Hospital.
*4:00–5:30 p.m. Anesthesia Conference. Dr. Etsten. Stearns Auditorium, New England Center Hospital.
*5:00 p.m. Surgical Journal Review. Mount Auburn Hospital, Cambridge.
*5:00–6:00 p.m. Service Meeting Followed by Clinical Conference (Medical, Surgical, Obstetrical). Faulkner Hospital.
*7:00 p.m. Some Problems of Bone Formation. Dr. Alexander Gutman. New Cheever Amphitheater, Dowling Building, Boston City Hospital.
8:00 p.m. Harvard Medical Society. Jimmy Fund Building, Children's Medical Center, 35 Binney Street.

WEDNESDAY, MARCH 9
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*9:00–10:00 a.m. Surgical Grand Rounds. Massachusetts Memorial Hospitals.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m. Orthopedic Grand Rounds. Bigelow Amphitheater, White 3A, Massachusetts General Hospital.
*11:00 a.m. Boston State Hospital. Psychiatry Seminar. Reception Building Auditorium. 591 Morton Street, Dorchester.
*12:00 m.–1:00 p.m. Clinicopathological Conference. Jimmy Fund Building, Children's Medical Center, 35 Binney Street.
*12:00 m.–1:00 p.m. Roentgen Diagnostic Conference. 5th-floor teaching unit, Beth Israel Hospital.
*12:15 p.m. Vascular Rounds. Drs. Edward A. Edwards and Chilton Crane. D-Main, Peter Bent Brigham Hospital.
*12:30 p.m. Weekly Pathological Meeting. Joslin Auditorium, New England Deaconess Hospital.
12:30–1:30 p.m. Weekly Staff Review of Autopsies. Dr. William A. Meissner. Joslin Auditorium, New England Deaconess Hospital.
*1:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*1:00 p.m. Massachusetts General Hospital Hand Clinic. The Clinics of the Massachusetts General Hospital.
*2:00 p.m. Rectal Clinic. Peter Bent Brigham Hospital.
*2:00–3:00 p.m. Pediatric Conference for Practitioners. Jimmy Fund Building, Children's Medical Center, 35 Binney Street.
*4:00–5:30 p.m. Fracture Lecture. Boston City Hospital.
*4:00–6:00 p.m. Overholt Thoracic Conference. Joslin Auditorium, New England Deaconess Hospital.
*6:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*7:30–9:30 p.m. Lahey Clinic Lecture. Joslin Auditorium, New England Deaconess Hospital.

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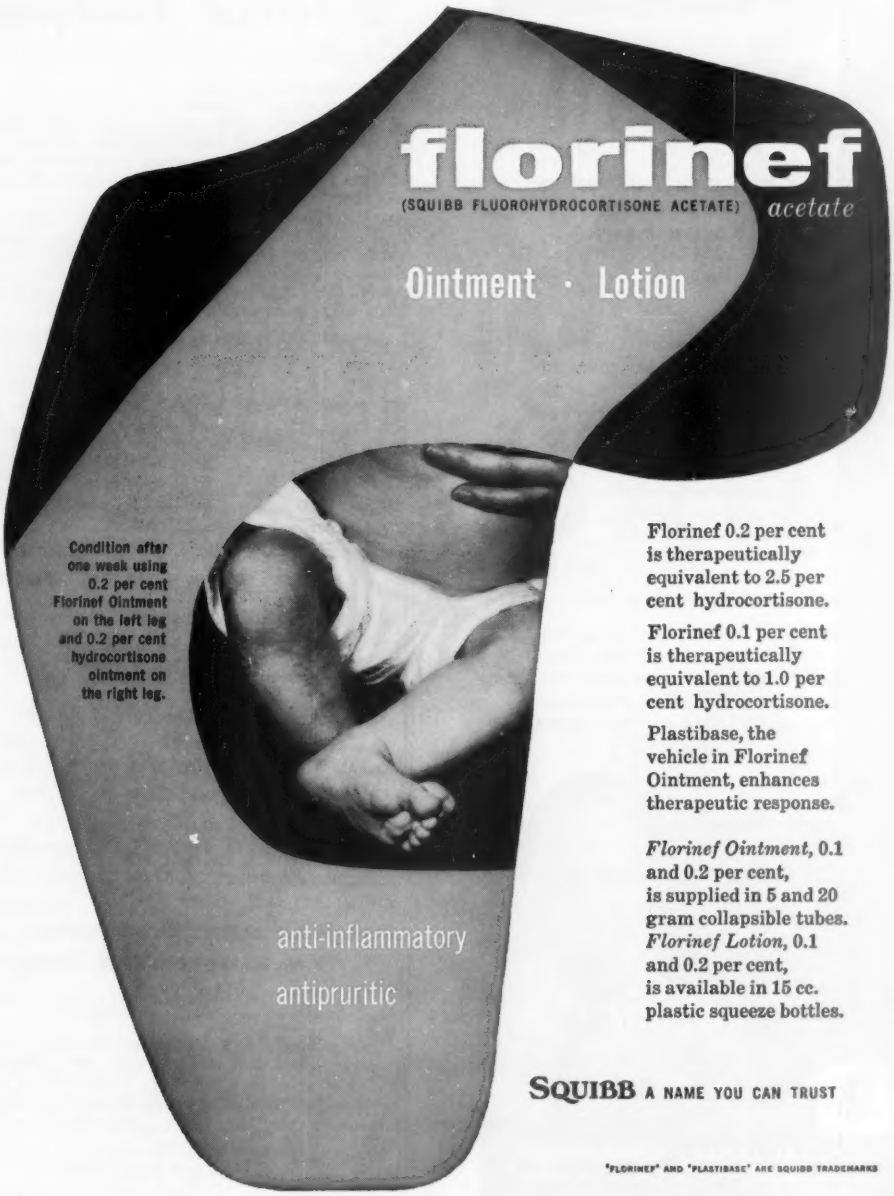

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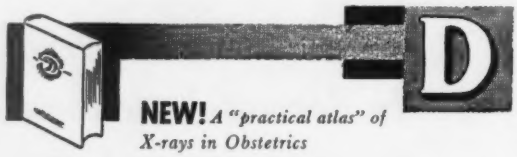

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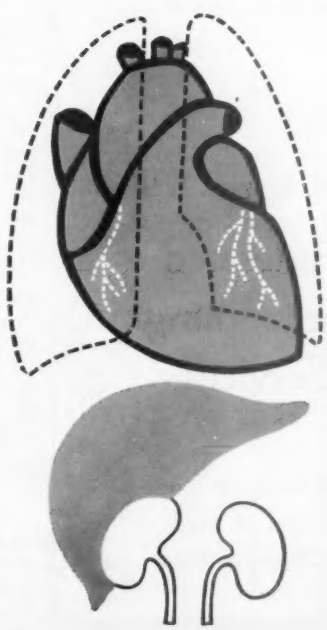

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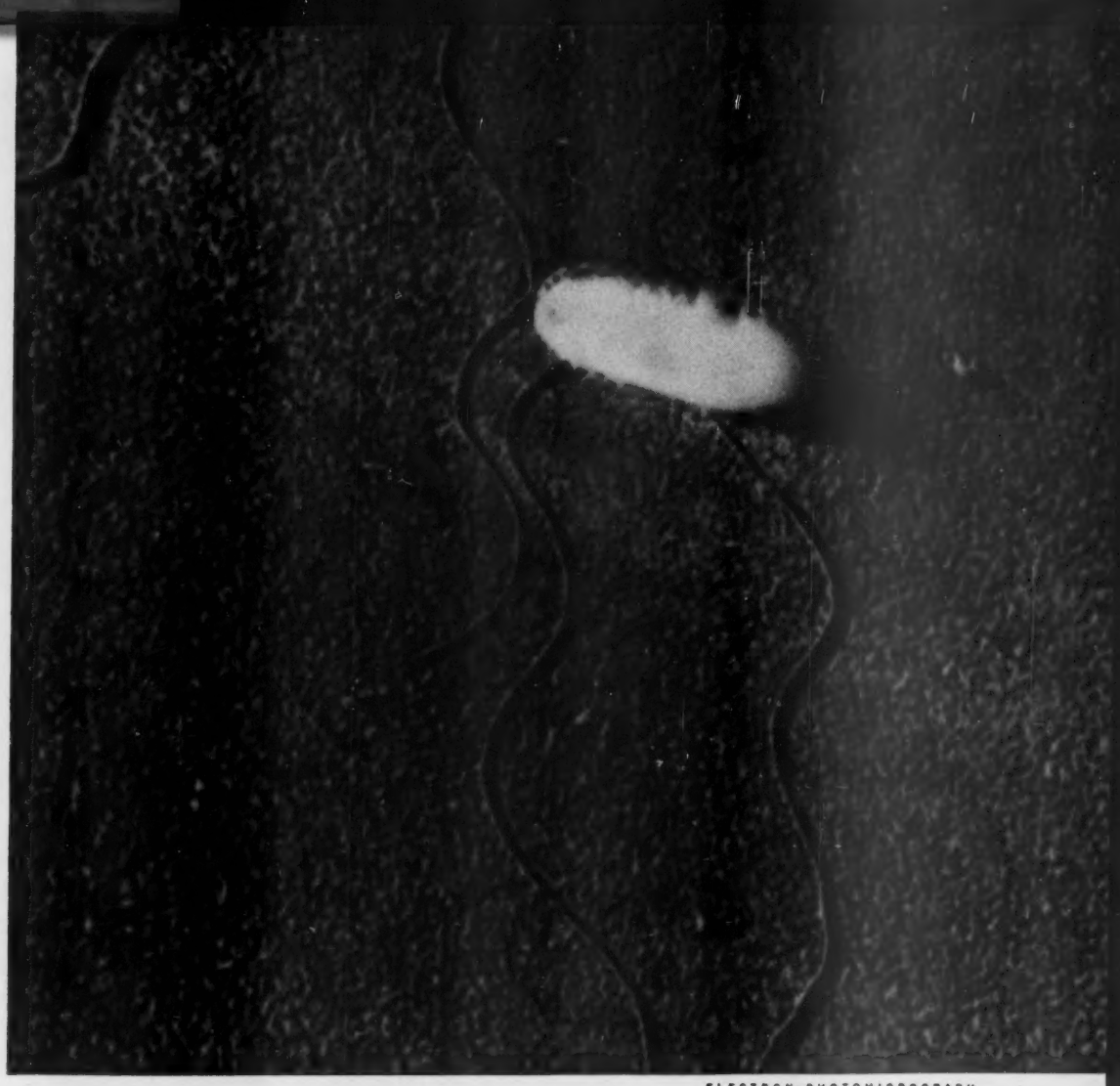

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of ammonium chloride
for your patients' convenience!

For samples just send your Rx blank marked — **26AM2**

Brewer
EST. 1852

BREWER & COMPANY, INC. WORCESTER 8, MASSACHUSETTS U.S.A.

Morrison, in treating a large series of patients with Maalox-Rorer, describes this better-tolerated preparation as "... a palatable, antacid, demulcent, nonconstipating colloidal suspension of magnesium and aluminum hydroxides, useful for the relief of hyperacidity."

This clinician concludes: "Magnesium aluminum hydroxide gel is more palatable than aluminum hydroxide gel and better suited to the prolonged administration required for the antacid therapy of peptic ulcer and hyperchlorhydria."[1]

A well-balanced suspension, notable for its smooth texture and pleasant flavor, Maalox has gained remarkable patient acceptance.

Supplied: in 355 cc. (12 fluid ounce) bottles. In tablet form, bottles of 100. Each tablet equivalent to 1 fluidram of the suspension.

Samples sent promptly on request.

maalox®
controls hyperacidity

1. Morrison, Samuel: Magnesium aluminum hydroxide gel in the antacid therapy of peptic ulcer, Am. J. of Gastroenterology 22:309 (Oct.) 1954.

ROER

WILLIAM H. RORER, INC.
Philadelphia 6, Pa.

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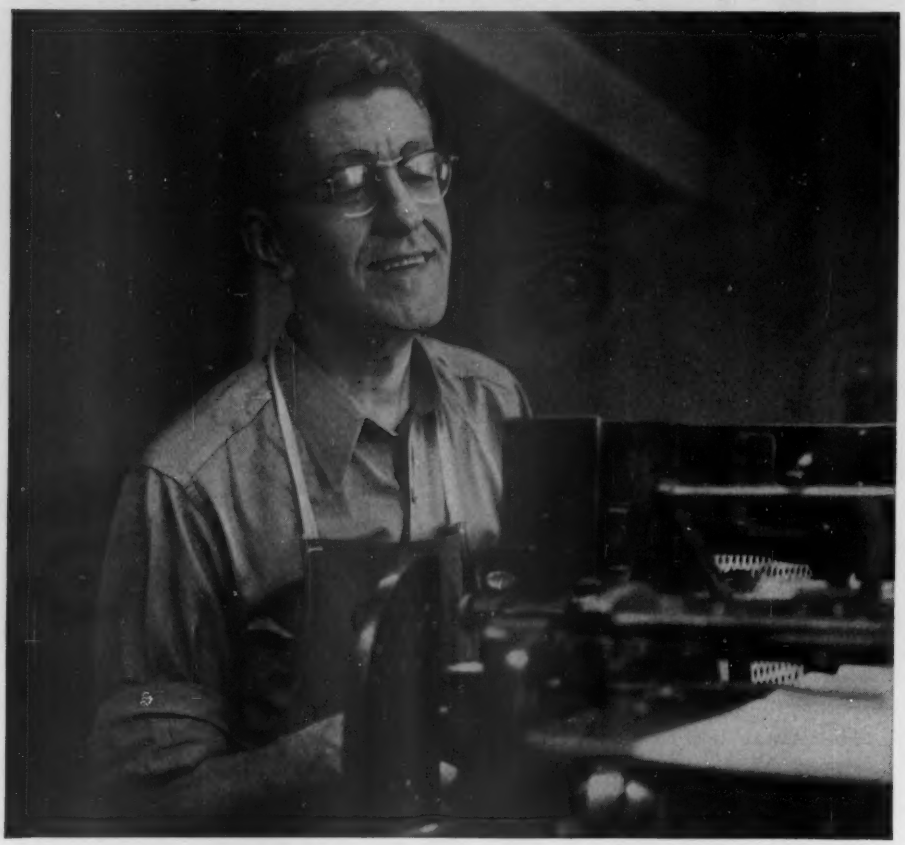
"Folks say I don't look 60. Well, I don't feel it, either!"



For many a spry oldster, the only change noticeable with advancing age is that each succeeding birthday cake has one more candle on it. To help such persons grow old gracefully, productively, and happily, a supplementary supply of vitamins and minerals may be desirable. GEVRAL* provides 14 vitamins and 12 minerals in one convenient capsule for geriatric use.

Gevral*

Geriatric Vitamin-Mineral Supplement Lederle

Lederle LABORATORIES DIVISION AMERICAN Cyanamid COMPANY Pearl River, New York

EACH GEVRAL *CAPSULE CONTAINS:*

Vitamin A (acetate)	5000 U.S.P. Units (125% MDR)
Vitamin D (viosterol)	500 U.S.P. Units (125% MDR)
Vitamin B_{12}	1 microgram
Purified Intrinsic Factor Concentrate	0.5 mg.
Thiamine Hydrochloride (B_1)	5 mg. (500% MDR)
Riboflavin (B_2)	5 mg. (250% MDR)
Niacinamide	15 mg.
Folic Acid	1 mg.
Pyridoxine Hydrochloride (B_6)	0.5 mg.
Calcium Pantothenate	5 mg.
Choline Dihydrogen Citrate	100 mg.
Inositol	50 mg.
Ascorbic Acid (C)	50 mg. (166% MDR)
Vitamin E (tocopheryl acetates)	10 I. U.
Rutin	25 mg.
Iron ($FeSO_4$)	10 mg. (100% MDR)
Iodine (KI)	0.5 mg. (500% MDR)
Calcium ($CaHPO_4$)	145 mg. (19% MDR)
Phosphorus ($CaHPO_4$)	110 mg. (14.6% MDR)
Boron ($Na_2B_4O_7 \cdot 10H_2O$)	0.1 mg.
Copper (CuO)	1 mg.
Fluorine (CaF_2)	0.1 mg.
Manganese (MnO_2)	1 mg.
Magnesium (MgO)	1 mg.
Potassium (K_2SO_4)	5 mg.
Zinc (ZnO)	0.5 mg.

MDR—minimum daily requirement for adults

Lederle offers a *complete* geriatric line including: GEVRABON*, a vitamin-mineral supplement liquid with a wine flavor; GEVRAL* Protein, a vitamin-mineral-protein powder; and GEVRINE*, a vitamin-mineral-hormone capsule.

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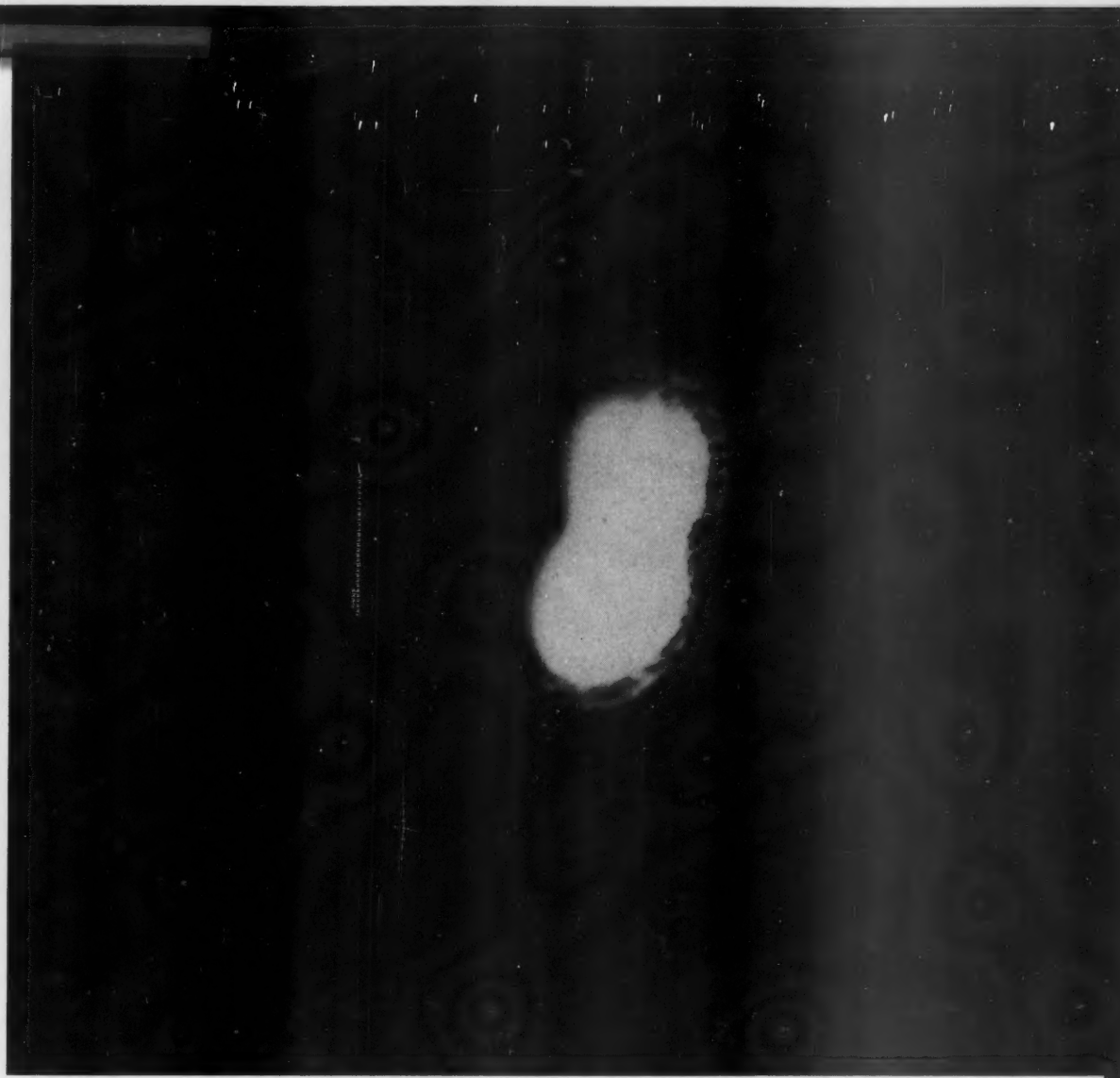

ELECTRON PHOTOMICROGRAPH

Diplococcus pneumoniae 44,000 X

Diplococcus pneumoniae (Streptococcus pneumoniae) is a Gram-positive organism commonly involved in

lobar—and bronchopneumonia • chronic bronchitis • mastoiditis • sinusitis otitis media • and meningitis.

It is another of the more than 30 organisms susceptible to

PANMYCIN*

100 mg. and 250 mg. capsules
250 mg./tsp. oral suspension (PANMYCIN Readimixed)

Upjohn

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Pleasant orange-tasting Vi-Penta Drops supply required amounts of A, C, D and principal B-complex vitamins for people of growing importance. Add to other liquids or give by the drop directly from the bottle.

In 15, 30, and 60-cc vials with calibrated dropper, *dated* to insure full potency.

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Relax the best way ... pause for Coke

Time out for refreshment

PHYSICIANS' Office FURNITURE. All standard lines, new. Used equipment from time to time. Convenient terms. Visit our showroom close by Veterans Hospital. Ample parking. T. J. NOONAN Co., 408 South Huntington Avenue, Jamaica Plain (Boston 30), Mass. Phone JAmaica 2-8700 for literature. Medical, hospital, laboratory, sickroom supplies. B260-20-tf

WILL SHARE beautifully furnished office, part time, on river side of Beacon Street. Commonwealth 6-0869. B199-7-2t

WANTED—Young man as assistant in General Practice in Boston suburb with view toward eventual partnership. Give full details of training and requirements. Address A191, *New Eng. J. Med.* 8-4t

COLONIC IRRIGATIONS, massage, diathermy. Beatrice M. Woods, 511 Beacon Street, Boston, CO 6-8722. B80-16-tf

DOCTOR'S SUITE ON FIRST FLOOR — Partly furnished if desired. Commonwealth Avenue near Dartmouth Street. KE 6-9230. B340-19-tf

BOARD INTERNIST, special training Cardiology, Harvard graduate, Boston-trained, desires association with practicing internist or group in New England, New York, New Jersey and Pennsylvania. Address A188, *New Eng. J. Med.* 7-3t

INTERNIST — Board eligible, university trained, married, age 30, due out of Navy early spring, desires position with established internist, or group, preferably in Northeast. Address A175, *New Eng. J. Med.* 4-tf

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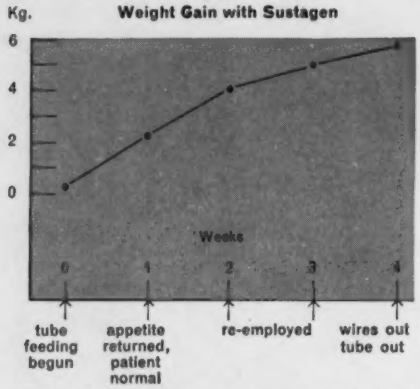
for seriously ill or malnourished patients.....

SUSTAGEN

complete therapeutic food for tube or oral use



Response to Sustagen in patient with jaw fracture. Jaw wired 4 weeks prior to Sustagen feedings; weight loss in that period, 5 Kg. (11 pounds).

aids and speeds recovery

This case is typical of those in a recent report* on 320 ill and malnourished patients given Sustagen feedings. All the patients achieved positive nitrogen balance . . . most of them gained weight . . . improved nutritional status often made needed surgery possible . . . bed-ridden patients became ambulatory . . . return to work was expedited.

therapeutic nutrition in therapeutic amounts

A 24-hour "diet" of 900 Gm. of Sustagen meets or exceeds the therapeutic nutritional recommendations of the Food and Nutrition Board of the National Research Council.†

Calories	3500
Protein	210 Gm.
Fat	30 Gm.
Carbohydrate	800 Gm.

Vitamins and Minerals:

Vitamin A	5000 units
Vitamin D	500 units
Ascorbic acid	300 mg.
Thiamine hydrochloride	10 mg.
Riboflavin	10 mg.
Niacinamide	100 mg.
Calcium pantothenate	40 mg.
Pyridoxine hydrochloride	5 mg.
Choline bitartrate	500 mg.
Folic acid	2.5 mg.
Vitamin B_{12} (crystalline)	4 mcg.
Iron (from ferrous sulfate)	15 mg.
Calcium	6.3 Gm.
Phosphorus	4.5 Gm.
Sodium	1.9 Gm.
Potassium	7 Gm.

Dilution for tube feeding:
1 cup Sustagen to 10 oz. water

Dilution for oral feeding:
1 cup Sustagen to 8 oz. water

†Therapeutic Nutrition, Publication No. 234, National Research Council.

by tube

Sustagen® is given easily and pleasantly with Mead's Tube Feeding Set, using small, smooth plastic tubing. Problems of discomfort and poor tolerance long associated with tube feeding are eliminated.

by mouth

Sustagen makes a pleasant tasting food drink. It can be used as a complete liquid diet or as a concentrated diet supplement for patients who cannot, or will not, take enough ordinary foods to meet their needs.

*Pareira, M. D.; Conrad, E. J.; Hicks, W., and Elman, R.: J.A.M.A. 156: 810, 1954.

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